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edited by M. L. Johnson *and*
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NEW BIOLOGY NUMBER 2

THE response to *New Biology No. 1* has encouraged us to produce a second volume. To new readers we should explain the objects of this publication. We aim at presenting discussions of modern aspects of biology in a form which assumes a little biological knowledge in our readers. Only by making this assumption can the articles be selves. Nevertheless, much of the volume's contents seriously scientific within the limits of space we set our- should be comprehensible to readers with no biological background. To assist such readers we have provided a Glossary of the main scientific terms which are used without explanation in the articles; and we hope that with its help *New Biology* will stimulate rather than daunt.

M. L. J.
M. A.

DEPARTMENT OF ZOOLOGY,
UNIVERSITY OF BIRMINGHAM,
March 1946.

THE WAR AGAINST RODENTS

By Anthony Barnett

THIS war began about 5,000 years ago. At that time men in Mesopotamia, and in the valleys of the Nile and the Indus, took to cultivating fields instead of temporary plots, and so began true agriculture. For the first time a surplus of food was produced beyond the needs of the producers: the surplus was stored against possible future disaster, or sent by land or water to towns, where again it might be stored.

The change in the mode of food production made populous human communities possible. Unfortunately, it also made possible much larger and more stable communities of several rodent species. It has been suggested that the worship of the cat in Egypt, 3,000 years before the present era, was a product of hostility to the rodents on which the cats preyed. It is at least certain that, when agriculture began, there were a dozen or so species of rodent, probably living a precarious existence in small scattered colonies, but destined to multiply many hundreds or thousands of times and to become largely or wholly dependent on man for their food.

Rodents are mammals, usually small and ground-living or burrowing, with clawed fore- and hind-feet, and teeth adapted for gnawing; the front teeth, or incisors, are prominent and very effective (look at Plate 8); the rest of the teeth are adapted for grinding; there are no canines or dog-teeth.

In Britain the rodents of greatest importance today are two species of rat, the house mouse, field mice (or 'voles'), squirrels and the rabbit. They are a nuisance or worse in two ways: they eat or destroy our food, and some carry disease to us and to domestic animals.

Rodents Destroy our Food. All the species mentioned so far are food pests. The field mice, squirrels and rabbits attack food whilst it is still in the fields, the rats and house mice when it is in stacks, granaries, ships and smaller stores down to private larders. In Britain we are comparatively free from the depredations of field mice. Our own species, *Microtus agrestis,* sometimes causes extensive destruction in conifer plantations, but that is almost all. But in the great agricultural areas of temperate Europe and Asia the continental field vole, *Microtus arvalis,* and allied species, have at times brought about such widespread destruction of crops as to cause disasters comparable with those due to swarms of locusts. Elton, referring to the outbreak of 1822, writes: "In that year Alsace was absolutely in the power of mice." And he quotes from a French naturalist: "It was a living and hideous scourging of the earth, which appeared perforated all over, like a sieve." Of vole plagues in general he says:

> This periodic upwelling of voles, the transfer of so large a share of human husbandry into the tissues of field-mice, is a process of terrific power. And yet we know so far very little about the process. There are several bare descriptions of the reappearance: how one year a few patches of abundance are noticed, coalescing to larger ones by the late summer and autumn, and how the plague grows serious next year and sometimes lasts over a third season. . . . Apart from the natural rhythm of decrease and recovery which operates in nearly all animal populations, we cannot at present suggest reasons for the widespread regional character of the outbreaks.

The story of the rabbit is more familiar. It is a sufficiently serious pest in Great Britain and other temperate countries of the northern hemisphere. Its introduction into Australia, as a useful source of food in a country which has little game for the pot, had a calamitous effect on the crops of certain areas. The rabbit, installed in a country-side offering plenty of opportunities, and containing no predators such as foxes or weasels, multiplied enormously.

The rodent pests most familiar, and most intimately associated with man, are the rats and house mice. They are pests of stored products, and are found in almost every human community.

Rodents Infect us with Disease. A variety of diseases which attack us are also, or even primarily, diseases of rodents. "It is a curious fact," writes Zinsser,

> that long before therec ould have been any knowledge concerning the dangerous character of rodents as carriers of disease, mankind dreaded and pursued these animals. Sticker has collected a great many references to this subject from ancient and mediæval literature, and has found much evidence in the folklore of mediæval Europe which points to the vague recognition of some connection between plague and rats. In ancient Palestine the Jews considered all seven mouse varieties unclean, and as unsuited for human nourishment as were pigs. The worshippers of Zoroaster hated water rats, and believed that the killing of rats was a service to God. It is also significant that Apollo Smintheus, the god who was supposed to protect against disease, was also spoken of as the killer of mice, and Saint Gertrude was besought by the bishops of the early Catholic Church to protect against plague and mice.

The causative germ of plague is a bacterium called *Pasteurella pestis*. This germ has as its principal home the members of various wild rodent populations. It is present, for example, in populations of ground squirrels in South-west Asia, and tarabagans in China. This infection of wild rodent populations not associated closely with man is called sylvatic plague. Very occasionally, a man or woman working in these areas may contract the disease. The danger is serious only when rats living in close association with man develop plague. The great outbreaks of the Middle Ages were, from a biological point of view, secondary consequences of epidemics among the rats of the affected areas. (The term 'epizoötic' is sometimes used instead of 'epidemic', where animals other than man are concerned. *Demos* means 'people', whereas *zoön*, or *zoion*, is a Greek word which can mean 'animal'.)

Plague is transmitted to man through rat fleas. An outbreak therefore requires not only the presence of the infection in a rat population associated with man, but also a certain level of flea infestation of the rats: rat fleas will attack man only when hard pressed for food.

Another widespread disease carried by rat fleas is murine typhus. (*Mus* is a general Latin term for rats and mice: hence 'murine'.) The great typhus epidemics are due, for the most part, to transmission by human lice; but the murine form of the disease is common in tropical and subtropical countries, where poor hygiene is responsible for the prevalence of this, as of other diseases. Scrub typhus, a similar disease of South-east Asia which has been important in the war against Japan, is carried by field mice and rats and transferred to men by mites.

There are several other rat-borne diseases of man which have been identified in more than one rodent species. Weil's disease, a comparatively rare and dangerous infective jaundice, is sometimes transmitted by rats to sewermen and miners, and to soldiers living in trenches: but the causative organism, *Leptospira icterohæmorrhagiæ*, has also been reported in the field mouse, *Apodemus sylvaticus*. Again, tularæmia is caught from rabbits in California, water voles in Russia and lemmings in Scandinavia.

These infections are usually assessed from an anthropocentric point of view. They are, however, also important to their other victims. For rats, plague is a calamity as it is for man. But the most disastrous rodent epidemics are those which end the great outbreaks of field mice and voles mentioned above. These always culminate in a catastrophic fall in the vole population, due to epidemic disease.

It was this fact that led to the excellent suggestion that the outbreaks might be controlled by a form of bacterial warfare. The germs were cultivated in artificial media, and baits were put down soaked in germ-laden broth for the rodents to eat. The results of this venture in biological control have so far been inconclusive. In general, nobody has yet shown for certain that it is possible to induce an epidemic in any rodent population. Moreover, some of these bacterial cultures are capable of infecting man. One species which has been used, *Salmonella œrtrycke,* causes an acute form of food-poisoning which is often fatal. The other main type, *S. enteritidis,* is less dangerous but is capable of causing disease in man nevertheless. In field mice these germs are not a serious danger to us any more than is the plague germ in wild squirrels; but, again as with plague, domestic rats (and in this case mice too) may also become infected and may pass the disease on.

Rat-borne disease is not always bacterial. Trichinosis is due to a nematode worm, *Trichinella spiralis,* which spends most of its life in a rat. We get the worm from pigs which have eaten infected rats. The disease has been relatively common in Germany, but in Britain it is exceedingly rare, perhaps because we do not eat imperfectly cooked pork Once, in Germany, when inspection and cooking failed, a single infected carcase caused 337 cases and 101 deaths.

This is enough to show, without reference to other diseases, that the rodent populations of the world constitute a reservoir of human disease which can, especially in areas where there are poverty and squalor, give rise to extensive and sometimes calamitous infections.

Men against Rats. In a war it is usual for each side to issue communiqués which give most emphasis to its own victories or successes. The same policy will be followed here. In the war of man against rodents man is mostly on the defensive: nobody has yet found a way of preventing vole plagues, nor are we in sight of exterminating the ubiquitous house mouse, *Mus musculus*. But the front against rats forms an exception: here there are some successes to be recorded, with a promise of more. Much of the rest of this article will therefore be on rats and their destruction. Successes have been scored against the rabbit too, but lack of space prevents an adequate treatment of that story.

There are two species of rat of world-wide importance. They both belong to the genus *Rattus* and are distinguished by quite trivial external features. *R. rattus,* the so-called black or ship rat (Plate 1), was the plague rat of the Middle Ages. It probably originated as a species in the south of Asia, perhaps in India or Malaya, but the regular transport of merchandise by ships (as well as by land) has enabled it to spread throughout the world. It is believed by some to have reached England in the thirteenth century, that is, at the time of the Crusades; it may have been introduced in the Crusaders' ships.

It became as familiar a pest throughout England as is the common brown rat today, and it is still sometimes called the 'old English black rat'. The term 'black' is misleading. Its colour is very variable, and in some parts of the world, particularly those with a climate warmer than that of Western Europe, the commonest form is one with a tawny back and a very pale belly. This is sometimes called *Rattus rattus frugivorus,* presumably because, in the country areas of sub-tropical regions, it is often found nesting in trees and feeding on the fruit. Farther north, however, in Britain for instance, *R. rattus* will live only in buildings. It is clear that it has been able to spread into temperate zones only as a result of the provision by man of warm habitations. *R. rattus* is primarily a climbing animal, and often enters buildings from the roof; unlike the common brown rat, it does not burrow, and does not swim readily either. In some parts of the world it commonly lives in the roofs of houses, and so is sometimes called *tectorum* instead of *frugivorus*.

In the Port of London and neighbouring districts it is usual to find *R. rattus* in the top floors and *R. norvegicus* in the basement and lower floors. All colour grades are here found together, including the variety called *alexandrinus*, which is grey. The *frugivorus* variety in these conditions seems to behave in the same way as the others, in spite of its special tree-climbing propensities in warmer climates.

Since *R. rattus* includes both black and pale varieties, with many intermediate forms, we need characteristics other than colour by which to distinguish it. The best of these are the very large ears, which are translucent, and the fine tail which is nearly always longer than the body; it is a lightly built rat, with a fine-pointed snout; and it does not usually reach a weight of more than 250 gm. (about 8 oz.).

The other important species of rat is *R. norvegicus* (Plate 2). (The name '*norvegicus*' is a mistake: there is no special connection with Norway). In temperate climates this species is even more of a menace than *R. rattus*. It spread over Western Europe early in the eighteenth century and seems to have reached England in 1728 or 1729. Once it had arrived, it was able to spread not only into human dwelling-places and other buildings, but also into farm lands, where it burrowed in hedge banks, ricks and any other suitable cover in the fields. For this is a burrowing animal: although it climbs well (not as well as *R. rattus*) it normally nests underground. Its underground habits have resulted in its general occurrence in sewerage systems: the expression 'sewer rat' means nothing more than *Rattus norvegicus* which happens to be living, or at least feeding, in the sewers. It did not originate in the sub-tropics, but probably in a temperate zone of South-east Asia: from this follows its ability to live in the open in Western Europe. Small colonies of this species have even been found living in cold stores in which the temperature is kept permanently below freezing-point.

R. norvegicus has smaller ears than *R. rattus,* and they are furry and not so translucent; its tail is relatively thick, and always shorter than the body; it is more heavily built, and it may reach weights of over 600 gm. (about 20 oz.), though individuals of more than 500 gm. are not common. The colour is nearly always brown, but there is a rare black form which makes it the more necessary to ignore colour when identification is being attempted.

The introduction of *R. norvegicus* into Britain (as in other Western countries) was followed by a decline in the numbers of *R. rattus*: this went on to about the end of the nineteenth century when *rattus* was a comparatively rare animal. Since that date, *rattus* has been increasing again, and in the last fifty years has become, probably, even commoner than *norvegicus* in the major port districts. It has also been spreading inland. This spread inland is mainly the result of transport by rail, or in lorries or barges.

It is not at all clear how these changes in the relative importance of *R. rattus* have come about. It is usually said that *norvegicus,* being a stronger and fiercer animal, has driven out the smaller species. The more recent spread of *rattus* makes it unlikely that this simple explanation can be correct. In the Port of London, at least in some areas, the majority of infested warehouses contain both species of rat. (Many of them—about 25 per cent—also have house mice: this disposes of the superstition that "where you have mice you won't have rats".

Although the two European species have a world-wide distribution, they are not the only important rats. In India and Burma, for instance, the place of *R. norvegicus* is largely taken by *Bandicota* (*Nesokia*) *bengalensis*, which not only looks like *norvegicus* but is a burrower of very similar habits. *R. rattus* occurs in South-east Asia, but shares the area with *R. concolor*, which is slightly smaller. In Java, the small size of *concolor* enabled it to nest in the hollow bamboo stems of which much of the furniture was made. The European colonists disliked sharing their beds and arm-chairs with rats and, being unable to get rid of them by more direct means, raised plantations to provide solid timber for furniture. After that the rats had to nest elsewhere.

We know much less about the habits of these other species and the control methods appropriate for them. The most successful investigations of rat-control methods have been carried out in England, and so apply primarily to the two species found there.

Research versus *Folk-lore*. It was war that stimulated the research on control methods. At the end of 1939 it was clear that the enemy would make great efforts to starve Britain. Large stocks of food had therefore to be accumulated, but were often stored in unsuitable premises, where they constituted an invitation to rats and mice which was eagerly accepted. A small body of research workers at Oxford had for many years specialised, under Charles Elton, the Director of the Bureau of Animal Population, in the study of wild populations. Their work had been what Haldane calls 'long-distance research', that is to say, it had never been designed to any immediate practical end. As soon as war broke out they transferred the whole of their energies to the study of the problems of the control of rats, house mice, and rabbits. For this purpose they were financed by the Agricultural Research Council.

At that time, the subject of rat control was pervaded with a mass of prejudice, folk-lore and mythology. There had been remarkably little serious scientific investigation, although, mixed up with all the nonsense, there were some good suggestions, just as, among the practitioners of rat or rabbit catching, there were some good men with extensive and valuable practical experience. One of the tasks of the research workers was therefore to clear away some of the undergrowth, and to expose and to put to the proof the good ideas that did exist.

As an example of the popular superstitions we may take the one that rat traps should not be handled unless gloves are worn: the reason given is that rats will avoid a trap smelling of man. This assertion was put to experimental test. Numbers of traps were put down in various places infested with rats, half of them after handling with gloves only and the other half with bare hands. Thus there were two identical sets of traps, each with an equal chance of catching rats, except for the single difference in the preliminary handling. The result was that both sets caught the same number of rats. A straightforward experiment thus disposed of what may be called the 'glove theory'.

Most of the research work, however, was of a more positive character. The aim was to establish methods for the complete extermination of rats in a given area. In the past there had been two methods which had been very extensively used: poisoning and trapping. It was established at a relatively early stage that trapping with the usual break-back traps was not an extermination method. The setting of very large numbers of traps relative to the rat population, a number, in fact, of the same order as that of the rats, produces a high kill at first and results, if the work is done with great care and thoroughness, in a reduction of the population to something like one-third of its original size. After that a few rats continue to be caught week after week for an indefinite period, but at such a low rate that the loss is fully made up by breeding (Fig. 1). A population which is thus immune to trapping is sometimes called 'trap-shy'. We do not know what trap-shyness is in terms of

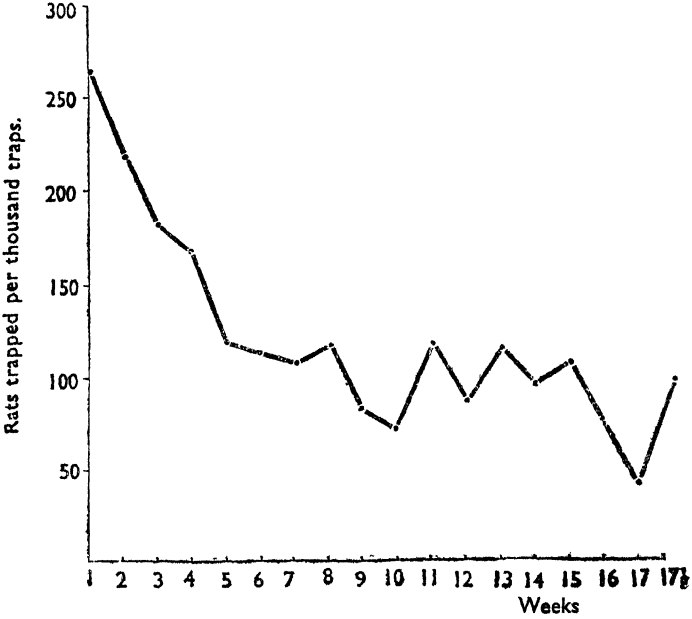


Fig. 1.—*The result of four months' trapping. After five weeks the number of rats caught per thousand traps set remains fairly steady and shows no further consistent downward trend.* (From M. T. Morgan *et al.*, *Preliminary Report on Rodent Control in the Area of the Port of London Health Authority* (1943).)

rat behaviour, but it is a very real phenomenon. The present writer once set eighty-six traps every night for a week, in a building well infested with *Rattus rattus*, and caught one rat. An employee had been setting traps intermittently there for the previous ten months.

These results of trapping illustrate the fact that, if extermination is required, the job must be done quickly. Any *chronic* method of control must clearly establish some sort of equilibrium in which the effects of the control method are balanced by reproduction. In *R. norvegicus* the average litter numbers about eight, and is produced after a gestation period of twenty-two days. The young remain in the nest for only three weeks, and are mature at twelve to sixteen weeks. Of course, there is always a high infantile mortality, but in favourable conditions a large rat population can nevertheless be built up very rapidly indeed.

Shyness and Avoidance. In view of the rat's formidable capacity for breeding it was fortunate that the second commonly used control method, poisoning, proved to be capable of giving complete extermination, at least in urban areas. There are, nevertheless, serious obstacles in the way of the aspiring rat poisoner. If poison baits are laid throughout an infested area, without any previous preparation, a number of rats will usually die but others will eat some of the poison but not die. (The proportion dying in these conditions varies widely, and may be nil.) The rats that have taken a sub-lethal dose will later decline the bait if it is presented again: such rats are said to be bait-shy (Fig. 2). (There is nothing unfamiliar about this to man: if we are made ill by a food, we generally avoid it afterwards, and without any ratiocinative process.)

The analysis of shyness has been a long-drawn-out affair, involving elaborate experimentation and analysis of the results. For practical purposes the important thing was the proof that rats may become shy, not only of a poison, but of a bait case, that is, the harmless part of the mixture.

It follows that if poisoning is carried out and leaves a residue of live rats, these must be attacked with a different bait base and poison.

It is, however, not sufficient to use the method of *direct poisoning*, that is, the laying of poison bait without any preliminary baiting. Observations on wild rats have shown that the effects of direct poisoning on rat behaviour are not simple. Rats, and especially the common brown rat, if left undisturbed display a preference for a regular daily routine. In an established infestation there is usually a simple pattern consisting of the nesting-sites, the feeding-places and the runs between them. These runs are often very well marked, and indeed provide the basis for the planning of baiting treatments. Plates 3–8 illustrate the traces left by rats; from such traces the experienced worker can plan the distribution of his baits so that some will be available for every rat.

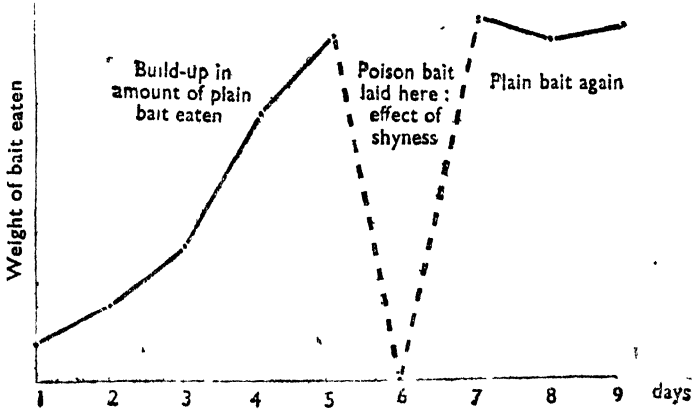


Fig. 2.—Daily take of bait by a rat colony. The curve illustrates two things. First, the daily increase in the amount of plain bait taken by the rats as shyness is overcome. Second, what happens when a poison of which the rats are shy is added to the bait; the amount taken falls in this case to zero. But the next night, with plain bait again, the full amount is eaten.

Let us suppose that we have under observation a regular rat run along the edge of a wall. One evening we place on it a small heap of wheat soaked in water, a foodstuff known to be acceptable. Rats emerge, begin to run along the wall, but before they reach the wheat swing out from the run and so avoid it completely. After a time, perhaps on the same night but perhaps later, they will approach the wheat and even nibble at it, but the amount taken will be very small. Only after a marked delay will the rats feed normally. If the wheat had been mixed with poison many of the rats, in their early nibblings, would have taken a sub-lethal dose: and this would have taken effect before any further bait had been ingested, feeding would have stopped, and the rats, once recovered, would have developed bait-shyness.

This avoidance response to change in the environment can be carried to startling lengths. On one occasion rats were nesting in a bank on one side of a path, and feeding in animal houses on the other side. In preparation for killing them sixteen empty boxes were set out on the runs at the edge of the bank. For three days afterwards not a rat was seen in the normal feeding-places. If this sort of thing happens when traps are put down rats are often given the credit for great intelligence. There is no justification for this at all. The rat is a conservative animal and automatically avoids the unfamiliar whether it is a palatable food, a harmless box, or something dangerous: such behaviour is the opposite of intelligent.

We have still to deal with the problem of the nibbling period in the response of rats to new food. If rats are to be poisoned effectively they must make a good meal of the poison bait. The solution to this problem is a simple one, though the work that led up to it was arduous and elaborate. It is to lay plain bait, that is to say, the bait base unmixed with poison, for a period of four to five days before laying poison. If the bait base is to be bread and water, this is laid alone, night after night, until the rats have become accustomed to feeding at the baiting-points and to making a full meal of the bait. (Fig. 2 shows the increase in amount of plain bait taken on successive nights. It does not, however, show what happens to the poison in a normal case.) After this the poison can be added and a kill of 85 to 100 per cent can be confidently expected. (Look at Plates 9 and 10.)

The extensive use of this *prebaiting* procedure has been the basis of the success of rat destruction in Britain during the war. The alternative would have been an attempt to find either so attractive a bait, or so powerful a poison, that the rats' avoidance would have no protective effect. In fact, during the war, no attempt was made to introduce more toxic poisons, and the evidence is that, even had this been done (with consequent further risk to man and domestic animals), it would still have been necessary to use the prebaiting method, at least with the bait materials that could be used in war-time. The poisons actually used are those which have been familiar components of rat baits for many years, namely, zinc phosphide, arsenious oxide ('arsenic'), and a plant preparation known as red squill.

Results such as these could have been achieved so quickly only by zoologists already in possession of a first-rate technique of investigation in the field. It was not enough to require the rigorous application of scientific principles, such as proper controls, adequate statistical analysis of numerical results and so on. If the research was to be of practical use it was essential that there should be a clear criterion of success for the control methods studied. The distinctive feature of the methods used at Oxford is an insistence on adequate census of the rat populations used in experiments.

Essentially, the census technique consists of the laying of an excess of a suitable bait (dry whole wheat was found convenient), night after night until the daily amount taken has risen to an approximately constant level. This level represents the size of the rat population at the time of baiting. Censuses carried out in this way, before and after an experimental treatment, make it possible to assess the effectiveness of the treatment.

The extensive use of this technique has made possible the confident assertion that the new methods can be relied on to give a kill of 85–100 per cent *in one treatment.*

Achievement. The application of the methods has been the responsibility of the Ministries of Food and Agriculture. It early became an urgent task to disinfest the Ministry of Food reserve stocks, and it is a remarkable fact that, by the middle of 1944, rats were a rarity in Ministry of Food depots and have never since been found in them in large numbers. It was, however, not enough to clear only Government-owned or controlled stocks. Rats on other ground were always a potential danger to them and were in any case causing immense loss of food elsewhere.

The destruction of rats in urban areas required the co-operation of the local authorities and of the general public. It was necessary to train members of public health departments in scientific methods of control, and to overcome lack of interest or deficient information among the people at large. The first has been done on a large scale by organised courses of instruction; the second, by exhibitions, posters, films and broadcasts.

One of the earliest, and quite the greatest of the achievements in large-scale control, was the campaign against rats in the London sewers. In the London County Council area there are about 3,700 miles of sewer, divided into two sections by the River Thames. The sewers of nearly every street were infested with rats. Presumably these were the two largest rat infestations in the world.

On December 6, 1943, the campaign began. Forty-four local authorities were involved; 1,150 men were employed. There are about 42,000 manholes in the area, and of these approximately 92 per cent were baited. Each area (with some minor exceptions) was given a first treatment of prebaiting with a moist biscuit meal followed by poisoning with zinc phosphide in the meal; a second, similar treatment was given with wet bread and barium carbonate. The whole campaign took ten weeks. The first treatment alone was highly successful: whereas 21,686 manholes showed take of poison bait in the first treatment, in the second only 13,717 showed take; and the amount of poison bait eaten in the second treatment was only about two-fifths of that taken in the first. It is known that big sections were completely cleared in the first baiting. L.C.C. sewermen working in the big trunk sewers reported that they hardly ever saw a rat after the campaign, although before they were constantly seen at every point. Two devices which played an important part in the campaign are illustrated in Plates 11 and 12.

Since the success in London the methods have been applied in nearly all the large built-up areas of England and Wales, and it has been clearly shown that, given the necessary organisation and labour, a similar success can be expected in any of the conditions encountered in them.

The importance of this work lies in the fact that the sewer rat does not confine himself to living and feeding in or near the sewers. In all large towns with old sewer systems the sewers are a constantly dripping reservoir of rat infestations, and many authorities have reported a sharp fall in the number of reports of rat infestations since the treatment of their sewers. Of course, it is not to be supposed that the sewers of London or anywhere else have been finally and completely cleared. Even if all the rats have been killed for the time being (which is not the case in most places), re-infestation will take place from above, since no city has yet completely destroyed its surface rat population. The work, therefore, has to continue, though with less expenditure of energy and materials than that involved in the initial campaigns.

Sewers are not the only 'reservoirs'. Certain trades inevitably provide conditions in which rat colonies numbering many thousands can develop. Glue factories using large quantities of offal are particularly susceptible. These, together with such sites as salvage destructors, abattoirs and municipal refuse tips, have been given special attention throughout England and Wales, and the results have shown that the new methods are equal to dealing with their rats.

In every county the Ministry of Agriculture has, during the same period, carried on the difficult task of rat destruction in the farms. A remarkable investigation by Middleton, of Oxford, carried out in a number of adjacent farms around an Agricultural Research Council establishment in Berkshire, has shown that intensive control can reduce the rat population of a large rural area to a level of less than one rat to every ten acres. At this level it is difficult to see any traces of rats at all by direct observation.

In Britain, rat destruction has been stimulated primarily by the desire to conserve food: rat-borne disease is in this country not of major importance. However, an outbreak of Weil's disease among coalminers in South Wales provided the occasion for the application of the new methods as a prophylactic against disease. It was found that quite minor modifications of technique made possible the successful use of the new methods against rats in coalmines. These rats, living mainly on the food provided for the horses, infect the miners with Weil's disease by depositing the germ with their urine: in wet conditions the germ may survive and enter a human being through the skin.

Abroad, however, rat destruction is in many places primarily a matter of the prevention of disease, notably of plague and murine typhus. As these words are being written the new methods are being used in Malta, India and Burma to combat plague: and in Italy, both to prevent plague and to preserve the precious stocks of food in a country in which starvation threatens.

The main reason why rat-borne disease is unimportant in Britain is that here, as in other countries of Western Europe, the United States and a number of others, the modern knowledge of bacteriology has been extensively applied: the level of the preventive public health services and of the organisation of public hygiene is far higher than it was anywhere in the world a century ago. It is not long since 'tropical' diseases such as typhus played a major part in filling the hospitals of London.

The development of hygienic habits represents a first step towards the universal application of scientific knowledge to human life; and it is important that it involves a certain level of general public education and co-operation: if we all threw our kitchen waste in the street and left our fæces indiscriminately in public places, we should have the sort of death-rates from typhoid, and from insect and rat-borne diseases, which are familiar in India, China and even Southern and South-eastern Europe.

The work described here is from one very small sector of the vast front of advancing knowledge and advancing application. Contributions to it have been made not only from above downwards: not only by the scientists who have told the rest what to do, but also in the reverse direction. There is a constant flow of questions and suggestions from those who may be called the consumers of the new knowledge and methods, back to those who produce them. The most frequently used bait base for rat destruction in Britain was first used by a junior, non-scientific employee of the Ministry of Food, and it was as a result of his suggestion that the research was carried out which proved this material to be outstandingly effective. Similarly, the sewer bait tray illustrated in Plate 12 was developed as a result of a suggestion by a sanitary inspector of one of the London boroughs.

This sort of two-way flow is going to be needed more and more during the period of reconstruction after six years of war. Bernal has said:

> One of the characteristics of the new age is that you cannot take a step in any social or political scheme without involving yourself in highly technical and scientific questions. It does not mean that scientists claim to be the Government or to have any other statutory position. It only means that government and administration are impossible unless they are thoroughly scientific, in the sense of having people in control who know what they are doing. We are very far from that position today. But it is coming and it is one of the duties of the scientist to point out that this process must go on very rapidly if we are to escape in this country the position of being relegated to a relatively barbarian status. (*The Times*, December 14, 1945.)

To this it may be added that the ordinary man and woman, and not only those 'in control', need to know what they are doing. This article may serve to illustrate, from one branch of applied zoology, the sort of thing that is required.

ACKNOWLEDGEMENTS AND FURTHER READING

The author and editors are indebted to the Bureau of Animal Population, Oxford, to the Agricultural Research Council and to the Ministry of Food for permission to use unpublished material and photographs. The reports of the Bureau, and that of the Ministry of Food Infestation Control on the destruction of rats and mice, should be consulted (when they are available) for further information on the subjects dealt with in the second half of the article. Modern control methods are described in *Infestation Control: Rats and Mice* (H.M.S.O., 1946). The method of taking a census of a rat population is described by D. Chitty in *Nature* (vol. 150, p. 59, 1942), and more fully in a paper in the

Journal of Mammalogy for February 1946, by D. Chitty and Monica Shorten.

For the earlier part, *Voles, Mice and Lemmings*, by Charles Elton (Oxford, 1942), is essential reading. For information on bacterial cultures, the paper by P. H. Leslie in the *Journal of Hygiene* (vol. 42, 1942) should be consulted. *A History of British Mammals*, by G. E. H. Barrett-Hamilton and M. A. C. Hinton (London, 1910–21), gives much information on the spread of rats, but is lamentably difficult to get. The quotation from Zinsser is from *Rats, Lice and History* (London, 1935), which deals with aspects of the history of some rat-borne diseases.

THE BIOLOGY OF SEWAGE DISPOSAL

By Ll. Lloyd

THE purification of sewage is a process designed to render harmless and inoffensive the organic waste produced by the community. Water conveyance of domestic waste from the dwelling was practised in the ancient civilisations of Crete, Greece and Rome as well as in Roman Britain, but this expedient fell into disuse in mediæval times. For centuries the growing towns allowed the refuse to be absorbed by the ground, or to accumulate in vast near-by middens, till the earth in their neighbourhood became saturated with excrement and urine which polluted streams and wells. Sewers were constructed below the streets, but were designed to carry away storm water only, and, being devoid of fume traps, badly levelled and with irregular flow, were not suited to take domestic sewage. Therefore, as the use of water-closets developed their contents were, at first, directed into cesspits below the dwellings, and these were cleaned out only at the rarest intervals. Of conditions in the early half of last century J. A. Delmege writes: "Discharge into the old sewers, moreover, was so tempting a way of disposing of excreta that their use for this purpose (not legalised till 1849) became more and more general, with the result that in all the larger towns, the rivers, often impeded with dams and weirs, now became nothing but lakes of sewage whose smell rendered their immediate neighbourhood almost unendurable." The Thames became a great cesspool, while the Serpentine was notorious as an open sewer and the small becks of provincial towns could sometimes hardly flow because of the accumulation.

Just as gaol fever, the louse-carried typhus, spreading occasionally to the general public, stimulated the reform of the prisons, so vast epidemics of cholera led to the establishment of sanitary authorities with the duty of discovering some means of rendering household waste innocuous. From both prisons and sewers the abolition of stench was the immediate aim, for this was associated with the idea of fever-laden air. The first step towards the scientific disposal of sewage was now made, for its discharge, untreated, into waters not tidal was forbidden. Unfortunately the law still allows careless authorities to pour any corruption into waters where the tide moves, regardless of whether the tide will carry it away, or swing it backwards and forwards in the lower reaches of the rivers, or deposit it on to pleasure beaches.

As no intensive system of purifying sewage was envisaged till the closing years of the nineteenth century the only available method of preventing untreated sewage from entering streams was its application to level areas of land into which it might slowly percolate and in its passage lose its harmful properties. Thus arose the *broad treatment* of sewage, which is quite a satisfactory method of dealing with the problem provided that a town has in its neighbourhood a sufficient area of fairly level ground of such porosity that it will absorb load after load of sewage, freed of course from its solid constituents which should be screened off and removed. It is still practised with success in some places, with or without the adjunct of farming, but in Britain suitable ground is rare in occurrence and limited in extent. Near Birmingham the soil was found suitable for absorbing the liquid portion of sewage at the rate of 500 people to the acre, so that this city would require a level of more than 2,000 acres of highly valuable land for a system of this type. In various places much ground that was quite unsuitable was employed, and the stench arising from ill-considered sewage farms is well within the memory of many of us.

From experience gained from the broad treatment, however, arose one of the first intensive methods of purifying sewage, the *contact bed.* This device is a bed of open stone some 6 feet in depth, either sunken in a pit or raised and walled in. Sewage runs in till the bed is full, remains in contact for an hour or so and then runs slowly out. The bed, wetted with sewage and the interspaces filled with air, is rested for a few hours and then filled again. Such beds fell into disuse because of their liability to choke up if the sewage was not pretreated to free it from all but the finest of solids. Methods of pretreatment had not then been devised. Many contact beds, moreover, were constructed with uneven, unwashed medium which readily impacted and prevented the free inlet of air when the beds were emptied. The contact bed is of interest because it formed the stepping-stone to the modern *percolating filter,* which is now the most commonly used device for purifying sewage. According to Sidney Barwise, this step was made by Colonel Ducat who, some fifty years ago, constructed a stone filter 8 feet in depth and distributed sewage evenly over it by means of iron girders which overflowed in trickles so that the filter was constantly and gently fed without for a moment interfering with the free movement of air in the depths. Just prior to this, the same author relates, Cameron of Exeter was the first to deal successfully with the sewage of a town. He treated the sewage firstly in *septic tanks,* a term he coined, and secondly in contact beds in which the products of the septic tanks were oxidised.

In those days the theory of sewage purification was little understood and indeed today authorities speculate as to what really happens in the percolating filter. It was known that certain bacteria had the power of liquefying all the organic solids in the household waste if this was allowed to stagnate in septic tanks for a sufficiently long time; that the liquid in such tanks became rich in the required bacteria so that further charges of organic matter would be more rapidly dealt with than the initial charge; that when matured by continued use they would deal with a steady intake of sewage and discharge water that was clear and relatively innocuous. This action consists in the breaking down of complex organic substances into simpler organic compounds of nitrogen, phosphorus and sulphur, and is caused by the feeding of various bacteria that can live in the absence of free oxygen, this essential substance being obtained by the bacteria from the food itself. This is the first stage in Nature's method of utilising dead organic matter. The next stage, which cannot take place in the septic tank, is carried out by other groups of bacteria which thrive only in the presence of abundant free oxygen, and they transform the products of the first stage and lead to the production of nitrates, phosphates and sulphates. These are stable substances which can in turn be used by plants. Cameron, with his septic tank and contact bed, separated the two processes into distinct phases and so achieved a greater speed of purification than unaided Nature can produce. The septic tank alone is satisfactory for the isolated house or the village community where the amount of effluent water is not great relative to the stream into which it flows. By itself it is indaequate for the town whose sewage discharges into a stream unless the stream is very large and swift. It is, however, still used in modified manner in many modern purification works as a prelude to the percolating filter, because it conditions the sewage very well for this further treatment.

It will be seen that the contact bed is outdated by more modern knowledge. In it the stones are left wetted by the sewage when the bed is emptied and the oxygenating bacteria can multiply in the sewage film. Then the bed is filled with the sewage devoid of free oxygen and the bacteria have to use their stored energy to stabilise the impurity. Thus, when they should be working hardest, they are deprived of the essential oxygen and work under a severe handicap, as it were 'out of breath'. In the percolating filter, on the other hand, the bacteria multiply as a film over the stones, the sewage is applied as a frequent film over this and oxygen is available all the time. Further, unlike the filter, the contact bed could not support an adequate fauna of grazing worms and insect larvæ (see below, pp 39, 45), as these are dependent also on free oxygen, and the filling of the bed with sewage would damage them.

In the modern filter system (Fig. 1) the *crude sewage* first flows into deep and narrow pits, the *grit pits,* where the fine stony material acquired by the sewage stream from the roads and other sources settles out in a retarded flow. The grit is removed from time to time and stacked on waste ground to dry. Next, mechanical screens catch and remove paper, vegetable peelings, rags and so on, and break up excremental masses. The *screened sewage* is then a turbid liquid with the solids in suspension finely divided. The filter cannot deal with all this fine solid matter, and it must be removed as far as possible either by liquefaction in septic tanks or sedimented out in extensive open pits, the *sedimentation tanks.* In these tanks the sewage should remain for some eight to ten hours, and some substance such as lime is often added to aid sedimentation. The *tank effluent* then flows to the filters. The sedimented *sludge* is removed from the tanks at regular intervals, pressed to expel excess of water, and used as a manure.

These extensive tanks have other advantages. The sewage flow is much greater by day than by night, though the plant can operate equally well at any time. Thus by suitable adjustments in capacity and design a more steady feed can be kept up on to a smaller area of filter than the maximum hourly flow would require. Secondly, sewage is

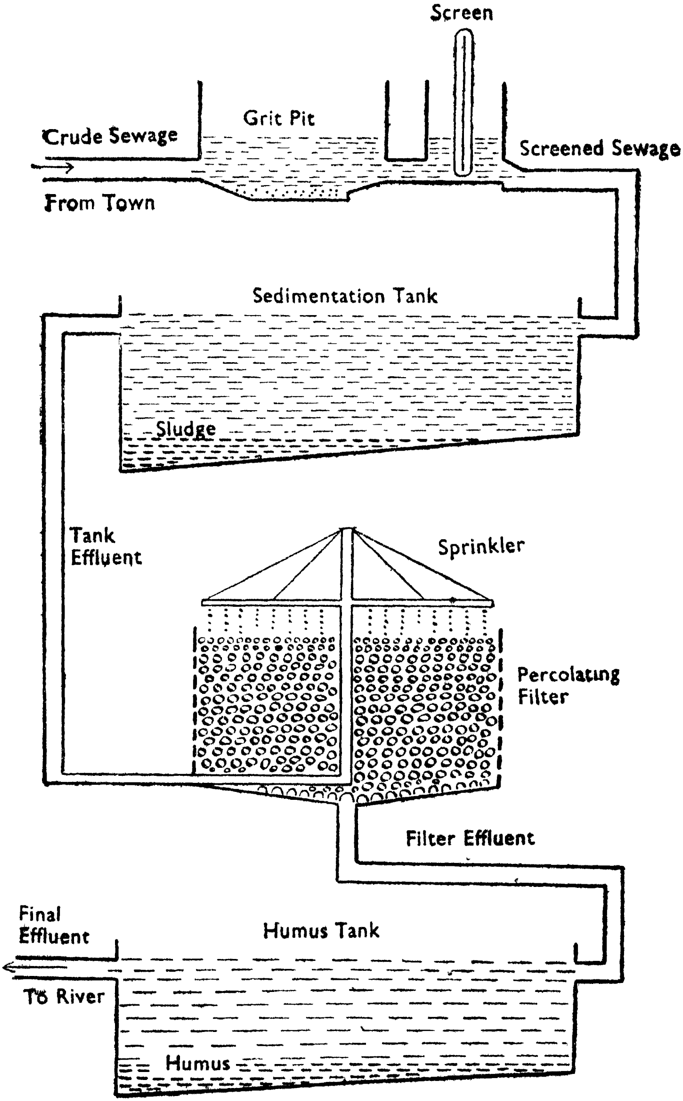


Fig. 1.—*Diagram showing the course of sewage through a system with percolating filters.*

not simply domestic waste but is also the product of practically every trade practised in the town, and the trade effluents are usually much more difficult to purify than is domestic sewage. Some, like the effluents from gasworks and chemical plants, are highly toxic to the organisms in the filters. It is most important that these effluents should pass through the sewage works and not directly to the streams, but the tradesmen rarely appreciate the problems of the sewage-works' operator and are loth to equalise their discharge through the twenty-four hours. Without the sedimentation tanks the denizens of the filter might at one hour be drenched with the alkali from a soap-works, at another with acid from a chemical plant, then with the tarry, poisonous waters from a gasworks. An industrial city like Leeds produces about 40 gallons of domestic sewage and 8 gallons of trade wastes per head per day. The more completely the 8 mingle with the 40 the better for the organisms of the filters, which can cope with anything the city produces but suffer from sudden changes of environment.

These considerations lead on to the question of the *strength of sewage.* Pure water saturated with air, as it is in a clean stream, holds in solution at ordinary temperatures about 1 part of oxygen by weight in 100,000 parts of water. If a certain quantity of such water were placed in a vessel and a certain quantity of sewage added the oxygen of the water would quickly disappear from solution, having combined with substances and organisms in the sewage. If the mixture were then agitated with air, sooner or later, according to the amount and strength of the sewage added, the water would again become pure and stable with the initial proportion of oxygen in solution. The added sewage has been purified by means of the ever-present bacteria with the aid of oxygen. Means have been devised of calculating how much oxygen a standard volume of sewage will require to effect its purification.

This varies according to the strength and constitution of the sewage and is expressed as parts of oxygen in 100,000 parts of sewage by weight and is called the *biochemical oxygen demand* of the sewage. The tank effluent of a city sewage works, as fed to the filter, has an oxygen demand of some 20 to 30 parts. To give this conception more general meaning it may be added that if ½ per cent milk is mixed with pure water and the mixture allowed to putrefy, it acquires a biochemical oxygen demand of about 40 per 100,000, and is thus a stronger 'sewage' than that fed to the filters of an average city.

Some trade effluents, such as the waste from dairies and milk processing, from beet-sugar factories and from fruit-canning plants, are too strong to be readily purified by the simple filter, and cause anxious problems at the purification plants of small towns where the bulk of domestic sewage is insufficient to dilute them adequately. Such wastes if untreated are more ruinous to streams than is domestic sewage itself.

The aim of the sewage-works' operator is to reduce the oxygen demand of the sewage to such a degree that the demand of the effluent on the water of the stream into which it discharges is practically nothing, and the officers of the Rivers Boards sample the final effluents from time to time to ensure that a proper standard is maintained. Thus one of the harmful effects of insufficiently treated sewage on the stream is that it depletes the oxygen of the water and may do so to such an extent that the animal life of the stream is seriously affected. Another and more serious effect is mentioned later.

The percolating filter, or *bacteria bed* as it is sometimes called, is usually 6 feet in depth and is filled with stone, clinker, slag or coke, according to which is most conveniently available, the requirements being that the material will not crush or fragment with frost. As regards the size of the medium, there is no final opinion as too few critical tests have been made. A surfacing with medium graded between 1 and 3 inches is usual, a larger grade being allowed in the depths. The smaller the medium the more extensive the area over which the purifying film can extend, but the larger the grade the better the supply of oxygen and the less likely is the filter to choke; as A. N. Barritt remarks, it is a question of striking a mean between these requirements.

The effluent from the sedimentation tanks, or septic tanks, is supplied to the filter by sprinklers which revolve or travel to and fro according to the shape of the filter, circular or oblong. In the first case the medium is wetted by a smaller charge at more frequent intervals and in the second with a heavier charge with a longer interval between the wettings, perhaps as much as twenty minutes or more. In English practice it is usual to feed the filters at the rate of about 1 million gallons to the acre per day, the *low rate* of application, so that a city the size of Leeds requires about 30 acres of filter. In recent years attempts have been made, especially in America, to speed up the rate of application so that smaller areas will suffice, and in these *high-rate filters* as much as 10 to 20 million gallons to the acre per day is applied. For some reason that is not understood rates of application between the 'low' and the 'high' tend to choke the filters; it is not simply a matter of the high rate keeping the filters flushed out. These high-rate filters have not the full efficiency of the low-rate types but prove useful in emergency, as in military camps, since they can be quickly constructed and occupy so much less space and they have the advantage that though flies breed in them (see below, p. 48) a large proportion of these nuisances is drowned in the rapid flow.

When first constructed the filter effects little or no purification but requires some weeks or months to mature by the growth of the complex association of bacteria on the medium. These bacteria multiply in a gelatinous matrix which is called *zooglœa,* but there are, in addition, forms which grow in filaments, and a number of species of fungi commonly develop also. On the surface of the filter filamentous algæ develop, and these are partly of the green type but mainly of the blue-green type, which especially thrive in waters where there is much organic contamination. The *film,* however, is by no means entirely of a bacterial and plant nature. It supports vast numbers of the single-celled animals, the protozoa, of many types. Some of these are anchored to the film and grow singly, or in branching colonies, while others creep or swim freely in the film of water that covers the gelatinous film on the medium. The protozoa may play an important part in purification, which will be explained later.

As the sewage continues to feed the organisms in the filters the film of zooglœa thickens and the mat of fungi develops till the closure of the interspaces is threatened; while, in some localities, the blue-green algæ, in an almost leather-like layer, tend to seal the surface. If these processes continued unchecked the filter would soon become choked and impermeable to the sewage, which would lie on the surface in a putrefying pool. However, the growth is checked by the feeding activities of worms and insects which live in and on the filter, constantly feeding on and loosening the film in fragments which are washed down by the trickle of sewage. Much of the film is converted into worms, or into flies which leave the filter, and much passes down into the effluent in the form of finely divided dejecta of the worms and insect larvæ. Thus the shedding of the film is a constant process, but because the activity of the worms and insects is related to temperature their grazing is lighter in winter than in the warmer weather, and during the former season the film gains greatly in thickness. Some time in spring, when a certain critical temperature is reached, the film being then thick and containing much dead material, the grazers develop great activity, and this causes the film to shed for a few days in a wholesale manner. This seasonal shedding is known as the *vernal slough.*

All these solids, from the disruption of the film, the dejecta of grazers, their dead bodies and the living forms that happen to pass out of the floor of the filter, get into the effluent. Even though the feed to the filter held no solids at all, and it is never free from some solids, yet the effluent from the filter must contain a lot. If the flow were direct from filter to stream then the stream bottom would become smothered in a fine organic mud. This mud, if present in sufficient quantity, covers and kills all green plant and most animal life in the stream as it lies in a putrescing layer. It is a greater evil than stream contamination by dissolved pollution alone, for the latter can pass on with the stream, but the mud bed once thickly formed remains for long, and each flooding of the current only serves to stir it up, release some corruption, and allows it to settle again. Therefore a requirement of the sewage works is that it shall discharge an effluent reasonably free from settleable solids as well as one with its oxygen demand satisfied. To effect this a further series of tanks is placed between the filters and the outfall. These are the *humus tanks,* in which the flow is greatly retarded so that the solids acquired in the filters, as well as any that may have passed through the filters from the initial charge, can fall to the bottom. These tanks are gently emptied from time to time, and the humus is cleaned out and spread over areas of level ground called *lagoons,* where it will slowly dry and become earth.

So far in this article the biological part in the purification has been attributed to the bacteria, and it has been proved in the laboratory that bacteria by themselves can achieve this end. It has, however, been recently suggested that in actual practice the protozoa play an important part, and they are certainly present in the filters in such abundance that some effect on the sewage seems sure. In order to build up an argument it is necessary to know something of a second system of sewage purification, that of *activated sludge.* This system was put into operation in Manchester by Fowler, Ardern, and Lockett in 1914. The sewage, instead of being brought into contact with air and purifying organisms in a thin film as in the percolating filter, is allowed to flow in long narrow channels and during its passage is violently agitated by paddles, or by injected air, and so tossed about that it is rendered frothy with air bubbles. It flows into tanks where solids settle out, and a proportion of these solids is pumped back into the aeration channels and mixed with the sewage at the beginning of its course. In time the solids change their nature and become cloud-like *flocs,* which consist very largely of zooglœal bacteria and protozoa. These flocs form the activated sludge and are the exact equivalent of the film in the filters. Part of the activated sludge is being constantly rejected, flowing to settlement tanks to separate out from the final effluent which goes to the stream, part is being constantly used again to supply to the sewage stream a sufficiency of the purifying organisms. The system has the advantage that it occupies much less space than an equivalent area of filter and a further advantage that it does not allow of fly breeding under normal circumstances, a thing inseparable from the filter system. On the other hand, it will not deal so well with strong sewages as does the filter system, and the very bulky surplus sludge is difficult to disperse.

The first operators of the activated-sludge system observed that great numbers of protozoa were associated with the flocs in the aeration channels and speculated as to whether these organisms might be an essential element in purification. It was found, however, that purification could proceed without them in small-scale model plants. So for many years the matter rested, but in quite recent times an increased interest has been awakened in the mechanism of sewage purification, and the question has been reopened, with interesting results. The protozoa dominant in activated sludge are of the ciliated type. The ciliates form one section of protozoa, the members of which move and feed by means of rows or spirals of numerous eyelash-like whips, the cilia, that beat the water and either drive the swimming animal along or draw a circulating current round the stationary organism, as the case may be. The members of the group characteristic of activated sludge are forms anchored by stalks, their bodies vase-shaped, with the cilia arranged as a spiral leading from the mouth on the free end of the cell. A vortex of water is caused by the cilia and this draws to the mouth bacteria and other minute food particles. They are known as the 'peritrichous ciliates', and the forms particularly dominant in the aeration channels are *Vorticella,* isolated on separate stalks, and *Epistylis,* growing in colonies on branching stalks. Two Indian workers, S. C. Pillai and V. Subrahmanyan, state that they have made cultures of *Epistylis* free from all bacteria and that these cultures with proper aeration can effect as much purification of the sewage as is performed by the activated sludge: that they have the power ot converting the dissolved impurities into stable, harmless substances and also cause bacteria to clump together into masses (flocculate), so that they sink more easily. When the bacteria have fallen out of suspension in this way the water becomes clearer and more sparkling, nearer to the ideal of the sewage-works' operator.

Various forms of protozoa have been shown by other workers to have this power of flocculating bacteria, and J. M. Watson has recently shown how it is exerted in one species of small ciliate, *Balantiophorus minutus,* and so, presumably, in all that exert this effect. He has discovered that this form pours a cloud of mucus from the region of the mouth and the mucus traps bacteria drawn in the current of water directed towards the mouth by the cilia. The trapped bacteria are thus removed from the water and swallowed. Some of the mucus escapes into the surrounding water, where it can be detected by adding special stains. This free mucus makes the bacteria sticky so that they adhere together in clumps and the cloudy water clears through their sinking. An analogous use of mucus is found in the nostrils of man and other mammals, where dust and bacteria are trapped and removed from the air entering the lungs.

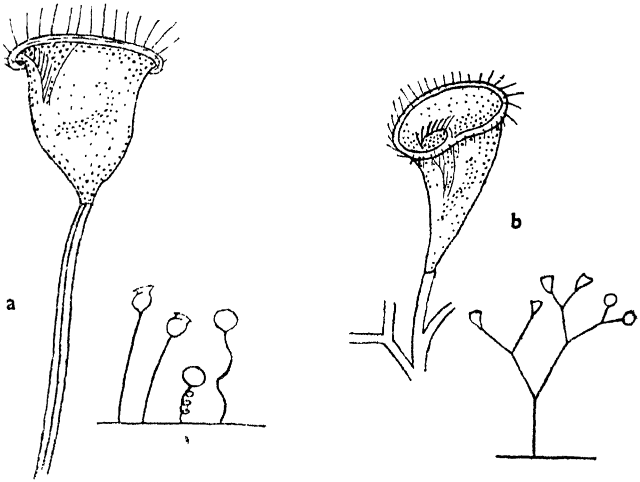


Fig. 2.—Protozoa found in activated sludge : (*a*) Vorticella, (*b*) Epistylis *A group of individuals* (*magnification* x50), *and a single individual* (*magnification* x350).

Science will not accept the ideas of the Indian workers *in toto* till their experimental methods have been searched by other investigators for some undetected flaw.

But, if they prove to be right in their revolutionary belief that protozoa, unaided by other organisms, can effect sewage purification, there is nothing antagonistic to the well-established fact that bacteria, also unaided, can perform the same function. A pasture may be grazed by a variety of animals and equally, it may be, a variety of organisms can remove the impurities from the sewage. In actual practice both classes, bacteria and protozoa, are present in vast numbers; a system without both is inconceivable, apart from small-scale laboratory tests very difficult to perform. There is, however, one ancillary function that can be attributed to protozoa which other organisms cannot perform. The aim in the mechanics of purification is to bring the contaminated water into as intimate contact with air as practicable. On each tiny unit of film in the filters and on each small floc in the aeration channels there are present abundant protozoa either swimming about or causing complex vortices in the water. These movements cause a turmoil and circulation in the water which no art of man could reasonably provide and the diffusion of oxygen to the smallest particle of sewage must be greatly aided by them; "their work was as it were a wheel within a wheel."

Modern purification of sewage is a centralisation and acceleration of processes that normally occur in nature, and the natural locality most closely resembling the percolating filter is the mud flat on the margin of a stream or pond. Such a flat is kept wet by seepage and occasional flooding and, especially when situated in woodland, receives on its surface a more or less regular supply of vegetable debris which, slowly disintegrating, is absorbed into the mud and finally reduced to simple salts. In and about such a mud flat many species of flies and other insects and many kinds of worms find all their requirements and play an important part in the dissolution of the vegetable matter. The worms *(Oligochæta)* in such places include several large species of the earthworm type and a number of species of small whitish worms which escape the notice of the ordinary observer. The flies include, especially, crane flies, hover flies, moth flies and midges of both a bloodsucking and non-biting type, all of several or many sorts. The worms and insect larvæ are very liable to get into the town drainage system by the overflow of ponds, while the flies, we must suppose, dispersed from their natural breeding-haunts by wind or their own volition, will often encounter sewage filters and regard them as akin in moisture and scent to their natural habitat. It needs no stretch of imagination to suppose that in one way or another every common mud-breeding species of worm or insect must often be taken to the filters and attempt their colonisation.

The mud flat may be regarded as a generalised habitat in that it affords very varied types of food, solid vegetable and animal matter of various sorts, alive and in various stages of decay, soft growths such as alga and fungus, and rich organic mud; various degrees of wetness, of exposure to sun, of depths in the mud, give different conditions; whether the animal lives on the surface or in the depths it finds firm bodily support. In the filters conditions are much more specialised, since the food available, apart from the worms and insects themselves, is a soft film-like growth or loose humus, and bodily support is available only to those forms capable of clinging against a gentle flow of water. In the filter, also, conditions change rather quickly with the drench at one moment and then the interval with the body exposed to air. There are other special features of the filter as a home for insects which space does not allow us to develop.

While no worms or insects that are not normally denizens of the mud flat have colonised the filters, the combination of special features makes them habitable to only a few of the many species that inhabit the mud.

For all practical purposes the successful colonists include only two species of oligochæte worms, *Lumbricus rubellus*, an earthworm, and a small whitish species, *Pachydrilus* (*Lumbricillus*) *lineatus*. Amongst the flies there are

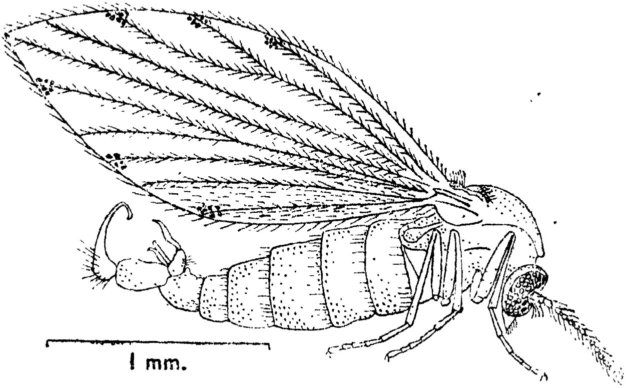


Fig. 3.—A moth fly, Psychoda alternata, *male.*

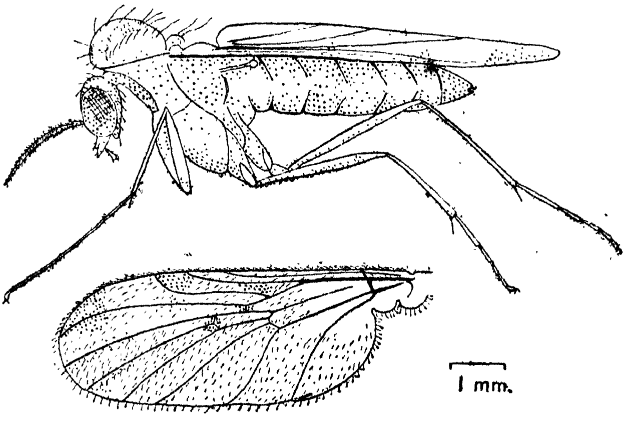


Fig. 4.—The window fly, Anisopus fenestralis; *below, a wing seen from above.*

three species of the moth flies, *Psychoda* (Fig. 3), the window fly *Anisopus fenestralis* (Fig. 4), four kinds of midges, viz. two *Spaniotoma spp.* and two *Metriocnemus spp.* (Fig. 5), and lastly a rather large fly, *Spathiophora sp.*, which catches and devours the smaller flies. Of other insects two sorts of springtail (Collembola) and a few insignificant beetles complete the list. Even this small quota of about fourteen sorts of mud-dwelling insects is not completed in all filters. There are two factors which especially limit it, viz. the strength of the sewage and the routine of operation. At Huddersfield, for instance, the sewage is so strong from the washings of wool and other chemical effluents that practically all forms are excluded except the hardy psychodas, and because these have no competitors for the food supply they abound there almost beyond belief. At some sewage works it is the custom to rest the filters in rotation for periods of a week or more, and this routine is adverse to *Metriocnemus spp.* whose larvæ and pupæ are close to the filter surface and so liable to death from drought; again the psychodas and *Spaniotoma spp.*, with no special proclivity for the surface life, benefit in abundance from their absence, for the filters keep moist in

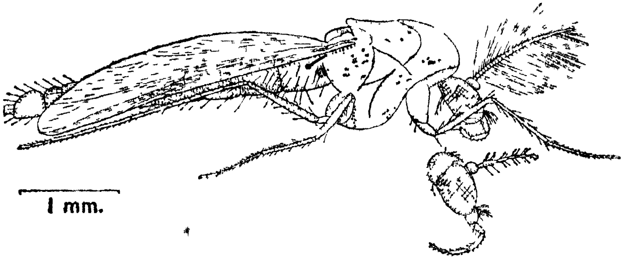


Fig. 5.—A sewage midge, Metriocnemus longitarsus, *male, and head of female.*

the depths. The window fly, though a very common insect, is found only locally in the filters, and the reason for its absence from many has not yet been discovered.

As remarked above, the efficiency of the filters depends on their maintaining an adequate fauna of grazing worms and insect larvæ, for without these they would quickly choke up and become worse than useless. Moreover, the grazing off of old, worn-out growth gives an opportunity for new, more vigorous film to develop. Their presence, however, introduces certain problems. The larger worms work particularly near the floors of the filters, and by burrowing in the humus that tends to lodge there prevent its accumulation, but, being so near the floors, they often pass into the effluent channels and reach the final tanks. Here they drown and putrefy till the humus is sometimes pink with their bodies, whose stench makes objectionable the weekly scouring of the tanks.

The flies that are successful in the filters while, and partly because, restricted in variety are produced in overwhelming numbers. In summer an output of some 40 million a day from each acre is not uncommon, and in favourable weather they may be seen like a continuous cloud over the whole filter surface. The midges are fairly strong-flying insects and keep reasonably near to the filters as a rule, but the psychodas and the window fly, *Anisopus*, are more feeble on the wing and so are readily carried by air currents to distances of half a mile or more from the works. They seek dusky places in which to rest, and so enter dwellings, sometimes in very great numbers, and cause annoyance because people living near the works know of their unpleasant origin. It is fortunate that none of the strictly domestic flies, such as the house fly and blow fly, can breed in the filters, as these insects are strongly drawn to the food of man and so infect the food with disease-causing organisms. The sewage flies take no interest in human food, with the single exception that *Anisopus* is attracted by the odours of a sink and has been known to lay its eggs on green salads. Though no association between the sewage flies and disease has ever been traced they often are a most serious worry to housewives. It is a great pity that the planners of towns have not always realised that the filter system of sewage purification is inseparable from abundant fly breeding, but have placed the works close to dwellings or have allowed new housing estates to approach their margins. Where proximity is imperative the activated-sludge system is to be preferred, as it is rarely associated with fly breeding and it has the advantage that it occupies less space.

The abundance and continuous output of flies from the filters are unequalled in nature for any equivalent area, and there are several reasons for this. In their natural haunts most insects in mud and similar materials have a strictly limited vertical range, but in the filters the depth of their habitable zone is relatively great and fairly uniform; the comparison of volume of breeding-ground is rather like the square against the cube. Secondly, the filter flies are all small insects and the individual larva requires little food. Thirdly, the food-supply is being steadily renewed the whole year through. Fourthly, these insects are all prolific, each female laying some two to six hundred eggs according to species. Fifthly, they are all rapid breeders, generation succeeding generation through the year, and in the filters there is no stern winter check so that the year will yield, according to species, four to eight generations, about double the number possible in a natural haunt in England. Fifthly, apart from some spiders, there are no strictly carnivorous forms to prey on the larvæ and pupæ, which are also protected from the ravages of birds except at the very surface. Lastly, the limited variety of species present tends to a greater total output of flies than in the highly mixed community of nature.

However, there is a certain amount of mutual destruction amongst the filter flies that tends to restrict the fly output. Where the filter fauna includes the full range of species that can inhabit the medium there is a smaller total fly output, and certainly a lesser nuisance, than where special conditions tend to limit the output to the psychodas. The larvæ of the midges have a semi-carnivorous habit, and in grazing over the film eat many eggs and pupæ and the feebler larvæ of the psychodas. In this activity the midge *Metriocnemus longitarsus* is of particular importance, for its vigorous larva dominates the topmost few inches of the filter when it is present in abundance and this region is naturally the one in which most of the eggs of all the species are laid. They act like a barrage against the other flies and the barrage is dense or diffuse according to the time of year and the particular qualities of the season.

It is known that one of the factors that keeps a certain check on insect abundance in general is found in vagaries of the weather, and an excellent instance is found amongst these flies. The generations of *M. longitarsus* are so timed that there is a big flight of the insects in mid-winter and the offspring from these emerge in May; the larvæ of the May flight are at their maximum activity in June. If June is hot and bright there is a heavy death rate, a catastrophic mortality, in this generation because of the impulse that forces the larvæ near the surface, for this dries up under strong sun in short cessations of the sprinkling; such intervals occur in any event for cleaning and oiling the sprinklers. Then the other larvæ, which are not drawn to the surface, or not strongly so, benefit from the reduction of their competitors. For the rest of the year, after a sunny June, the barrage of larvæ that *M. longitarsus* forms near the surface is thin and the eggs of flies placed in this zone are less likely to be destroyed. Conversely, after a cold, wet June the barrage tends to be denser for the rest of the year and there is more egg destruction.

Another instance of evident competition in the teeming life of the filters is to be found in winter behaviour. It has just been mentioned that *M. longitarsus* has a winter flight, and so also has one of the psychodas, *P. severini*, though the other psychodas are more restricted to warm weather. It might be supposed that these two winter-breeding flies would benefit when the winter was mild because the feeding and progress of insects in general is proportional to temperature. It has been found, however, that they tend to be scantier after a mild winter, more abundant after a cold one. This anomaly is explained by the behaviour of the small worm, *Pachydrilus* (*Lumbricillus*) *lineatus*, studied by T. B. Reynoldson. This worm occurs in vast numbers in most filters, and in a few cases is so abundant that its clusters choke the filters and impede the flow of sewage. It likes to work just below the surface, but is forced to greater depths by cold. In a mild winter its masses can remain constantly in its preferred zone unharmed by the feeble sunlight, and thus it competes for food more strongly under such conditions with the surface-loving insect larvæ. It breeds particularly in the cooler months, and when the filters retain a temperature of 10° C., as they will in a mild winter, it can achieve one generation and start a second. But in a cold winter, when the filter temperature falls and remains at 5° C. or below, the worm cannot complete one generation during the cold months. Therefore after a cold winter it is a less active competitor for the food required by the insect larvæ than it is after a mild one, and the effects of this competition are reflected in the abundance of the winter-breeding flies in spring.

It is generally acknowledged that one of the strong guiding factors in evolution is competition between species, but the evidences of this force are not easy to study in open nature, where there is difficulty in analysing conditions and in assessing populations in the lower animals. Conditions can be analysed, and reasonably accurate assessments of population made, in the filters, and so the mechanism of competition can be deduced. Further, when the mechanism of competition is understood, we are better able to understand that the important differences between closely allied species are not those points in form and colour by which we distinguish and name them but differences in habit, reactions to the physical forces in nature, which are linked and inherited with the more evident distinctions. For these reasons the studies on the fauna of the sewage filters, carried out by various workers at the University of Leeds, have an interest for biologists quite apart from the purification of sewage.

FURTHER READING

J. A. Delmege, *Towards National Health* (London, 1931), traces the development of sanitary sense up to the year 1875.

S. Barwise, *Purification of Sewage* (London, 2nd ed. 1904), continues the history up to the development of the percolating filters.

Several technical works give details of modern practice, as T. P. Francis, *Modern Sewage Treatment* (London, 1931).

No account of the biology of sewage purification has been collected in volume form, but original articles may be found from 1935 onwards in the following journals :

Annals of Applied Biology.
Journal and Proceedings of the Institute of Sewage Purification.
Sewage Works Journal (U.S.A.).

WHALES

By R. F. Ewer

WHALES have long been of interest to man for economic reasons. They supplied him with oil for food and for lamps, and later various uses were found for the whalebone. Its rôle as a stiffener in ladies' corsets and its use for the handles of various articles, such as whips and backscratchers, is well known. Whalebone was also used in the thirteenth century to make plumes for helmets, and it was the incorporation of thin shreds of whalebone which gave to the once fashionable heavy silks the power to 'stand of themselves.' No doubt whaling had its origin simply in taking advantage of any animals unlucky enough to be cast ashore and stranded, but from this to deliberate hunting is not a long step. The large size of the quarry necessitated the development of special weapons. The harpoon was a variation of the spear, with retaining barbs and a line attached; later came the harpoon gun. The whaler must, of course, first find his whale then kill him, and the finding may be a slow and chancy affair. Today the methods which were developed for locating enemy aircraft and submarines are being brought to the whalers' aid, and may greatly reduce the time spent in searching for the animals.

As long ago as 1197 whaling was sufficiently developed in Europe for King John to levy a tax on all whales landed. Improved methods of hunting led to the growth of an important industry, which reached a maximum in the first half of the nineteenth century. Towards the end of the century there was a set-back—the demand for oil was greatly reduced by the development of alternative forms of lighting: gas, paraffin and finally electricity (Swan produced the first carbon-filament electric-light bulb in 1877); and it was found that metal could mould the female form just as effectively as whalebone. The following prices for sperm whale oil are eloquent of the declining market:

1866—$2·75 per gallon.
1872— 1·56 „ „
1882— 1·10 „ „
1890— 66 cents per gallon.
1900— 45 „ „ „

The industry has been re-established as the result of advances in our knowledge of the chemistry of fats. It was found that by hydrogenation oils can be converted to fats, and hence whale oil can provide us with margarine. The species which are now the most important commercially are the blue whale, the fin whale, the humpback, the sperm whale and the sei whale. Modern whaling is carried out mainly in the Antarctic Ocean; the northern fisheries are much less important. The northern whale stocks may never have been as large as the southern, but their present secondary position is largely due to the unrestricted hunting which went on in the nineteenth century. The Greenland right whale, for instance, was hunted almost to extinction by the end of the century, but there are indications that it is now on the increase again. In 1938-9, the last season for which figures are available, over 36,000 whales were killed, and these produced two and a half million barrels of oil. One whaling factory ship which left England this year hopes to catch in the course of the season enough whales to provide a million people with a year's margarine ration.

Whales are of two sorts, differing from each other in many important respects, the *Odontoceti* (toothed whales) living on large prey, and the *Mystacoceti* (whalebone whales), which are plankton feeders. The *Odontoceti* include the dolphins and porpoises, the killer whale, the narwhal, the bottlenose and the sperm whale. The killer feeds largely on other whales and seals, but fish too are taken; the sperm whale eats cephalopods, and the others live on fish. The teeth of the *Odontoceti* are unlike those of land mammals: there is no differentiation into incisors, canines and chewing molars; all are alike conical and pointed, adapted for holding but not chewing. The prey is swallowed without mastication, whole if not too large or just slashed into lumps. Correlated with this the lower jaw is weak, and the muscles usually used in chewing are poorly developed. Mastication under water is scarcely desirable, as active and slippery prey would stand a good chance of escaping in the process.

The *Mystacoceti* include the 'right whales' (so called because they used to be the species most hunted and so were 'right' from the whalers' point of view), the rorquals or fin whales and the humpbacks. They grow to a much larger size than the *Odontoceti*, but their food consists of small Crustacea, about the size of shrimps, the 'krill' of the whalers. In polar seas these Crustacea occur in vast numbers, and the whale strains them out of the water through the baleen. Although called 'whalebone' the baleen is not really bony, but is developed from the lining of the roof of the mouth, and is more comparable with nails and horns. It consists of elongated plates which taper away to a point and are frayed out into fine fringes at the bottom and inner edges; the whole acts as a filter, retaining the krill and allowing the water to flow out of the mouth. Baleen is quite different from teeth, which are never found in *Mystacoceti*, but the fact that their ancestors had teeth is shown by the vestiges of tooth germs that occur in the embryo but never develop far enough to cut the gums. That the largest of animals should feed on anything so small cannot fail to excite our wonder, as it did John Evelyn's in the seventeenth century. In his *Diary* he describes a whale which came up the Thames and was killed near Greenwich and "drew an infinite concourse to see it, by water, horse, coach, and on foot, from London and all parts." He concludes by describing how "the extreamës of the cetaceous bones hang downewards from the upper jaw, and was hairy towards the ends and bottom within side; all of it prodigious, but in nothing more wonderful than that an animal of so great a bulk should be nourished only by slime thro' those grates."

The most fascinating thing about whales, however, is that although they are born in the water, spend all their lives there, find their food there and mate there, they are nevertheless mammals—although so wonderfully adapted to life in the water they did not begin their history there, but are the immediate descendants of land animals and have gone back to the home of their remote fish forbears. When we watch a dolphin playing round a steamer, swimming with such effortless ease, although we know it is not a fish we can hardly help feeling that it ought to be one. The alterations both in structure and in physiology which have accompanied this transition from land back to water make an interesting evolutionary story, and it is with these adaptive changes that this article is mainly concerned. This readaptation of a land mammal to water can best be understood if we consider the difficulties that will be met, the problems that arise and how they have been solved. Locomotion, respiration, water balance and reproduction are the functions mainly affected, and each will be treated separately.

Locomotion. The most efficient method of swimming is that used by the fishes, sculling with the tail. For maximum efficiency the body should be streamlined so that eddy-formation and consequent drag are at a minimum. For the same reasons swimming is more efficient completely submerged than awash, for at the surface considerable turbulence will inevitably be caused. The energy necessary to drive a 75-foot whale along at various speeds has been calculated by Barcroft to be as follows:

Speed (knots)	*Horse-power at surface*	*Horse-power submerged*	*Ratio H.P. surface/ H.P. submerged*
5	12·2	7·5	1·6
10	243	53·5	4·5
15	1775	168	10·5

The advantage of complete submergence is considerable, especially at high speeds; at five knots the energy required to swim at the surface is about one and a half times what is required submerged, and at fifteen knots it is over ten times.* Gray determined the force necessary to pull a model whale through the water, and from the weight of the swimming muscles in the animal calculated that the muscle must be capable of developing ·07 horse-power per pound. Trained athletes and dogs can produce ·01 horse-power per pound of muscle: this would seem to imply that whale muscle is seven times as efficient as that of other mammals. But these calculations were made on towing a rigid model which does form eddies. Gray showed that if instead of being rigid the hinder end waggles, as a whale's tail does in swimming, then eddies are much reduced, and a calculation taking this into account brings the necessary horse-power down to the same value of ·01 per pound of muscles. The whale's muscle is quite normal.

* A submarine, of course, can travel fastest when it is at the surface. This is partly because it then uses internal-combustion engines which are more powerful than the electric ones used when it is submerged; but it is also because the submarine, unlike the whale, is not very well streamlined. The resistance to the water caused by the gun and conning tower more than outweighs the advantage gained by avoiding turbulence due to breaking the surface.

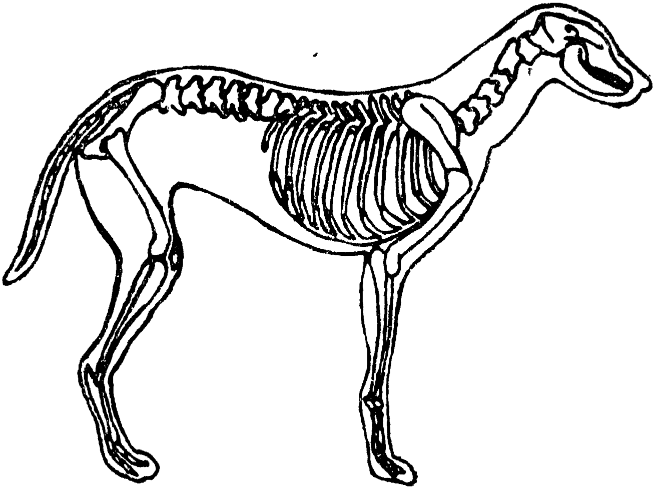
Another factor involved in swimming efficiency is surface friction. The frictional drag will be proportional to the size of the surface in contact with the water. Provided a body is kept the same shape, the larger it is the smaller will be its surface area in proportion to its volume.* This means that since the whale's muscles will be proportional to its volume, the bigger it is the smaller will be the frictional force to be overcome per pound of muscle available; large size makes for economical swimming.

Bearing these points in mind we can see how admirably the whales are adapted for swimming. Large size they certainly possess. Whales include not only the largest living animals, but the largest animals that ever lived. The blue whale is the biggest species; it reaches a length of 100 feet and weighs 160 tons, the equivalent of forty large elephants. Even the largest Dinosaurs fell far short of this; *Brontosaurus,* the heaviest, has been estimated to have weighed thirty tons, while the longer but more lightly built *Diplodocus* was only 87½ feet long. The body is most effectively streamlined, all contours are rounded with a padding of blubber and the hair has been lost. All external projections have gone, except one pair of flippers for balancing and steering and in many cases a stabilising fin on the back. The hind limbs have been lost altogether in the *Odontoceti,* and are represented in the *Mystacoceti* only by vestiges which do not project externally. The external ears are gone, and in the male the penis is completely retracted. The neck region is abolished, and the head flows smoothly into the body without an abrupt contour change. The whale swims submerged, and the propulsive organ is the tail, just as in the fishes, but with one important difference. In fishes the main part of the

Consider a cube with sides 1 inch long, and another with sides 2 inches long. The first will have a volume of 1 cubic inch and six sides each 1 square inch: the second will have a volume of 8 cubic inches, and six sides each 4 square inches. For 1 cubic inch of volume the first cube has 6 square inches of surface, the second only 3.

propulsive stroke is horizontal and the tail is flat in a vertical plane, whereas in whales the flukes are horizontal and the propulsive stroke is vertical. The up and down stroke is of advantage to an air-breathing animal, for it enables it to reach the surface very rapidly when in need of a fresh supply of air. This is as desirable for aquatic reptiles as for mammals, and one naturally asks, why, then, did the extinct Ichthyosaurs, a group of marine reptiles, swim with a side-to-side stroke like a fish? The answer is a historical one. The primitive vertebrate locomotory movement is the horizontal bend of the fishes. The first amphibia came ashore with it, and although they and the reptiles crawled they assisted the movements of their limbs by bending the body from side to side, and even modern newts and lizards walk with sinuous horizontal body-bending movements. When a reptile returned to water it did so with a neuromuscular equipment still biased to the horizontal direction, and naturally swam with the main movement in this plane. This was not true of the mammals. Their terrestrial locomotion has become completely emancipated from the original body bending, and indeed in fast movement the bringing forward of the hind legs is often assisted by bending the back in the vertical plane; a dog galloping shows this very clearly. When the ancestors of the whales returned to the water they were therefore in a position to develop something new in vertebrate locomotion, swimming by an up-and-down stroke.

This change from land to water locomotion has been accompanied by many modifications in the skeleton besides the loss of the hind limbs already mentioned. The fore limb has been converted into a steering paddle by a great flattening of all the bones. The hand region, forming the flat of the paddle, is enlarged by an increase in the number of finger joints, while the arm is very much shortened so that the paddle is close to the body. The bones are firmly linked together and the power of individual movement of one bone on another is lost: the limb moves as a whole from the shoulder-joint. The shortened neck is achieved not by reducing the number of vertebræ—the seven characteristic of mammals (even the giraffe) are still there, but are flattened and telescoped together. The up-and-down swimming stroke requires a slightly new arrangement of muscles. A fish has its muscles divided into blocks running one on each side of



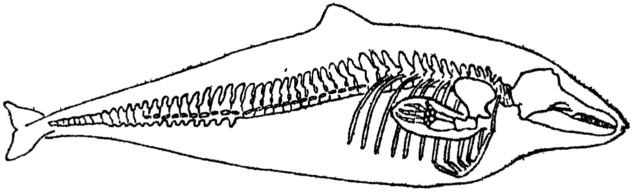


Fig. 1.—Above: outline and skeleton of a dog. Below: outline and skeleton of a porpoise. Note the fish-like shape, short neck, absence of hind limb, fore limb forming a flipper, horizontal tail flukes and fin on the back.

the spine, and by alternate contractions they move the tail from side to side. The vertical stroke necessitates a further splitting of these blocks into upper and lower sections. This in turn demands extra anchorages, and to provide the necessary attachments for these muscles the transverse processes on the lumbar vertebræ have been greatly increased in size.

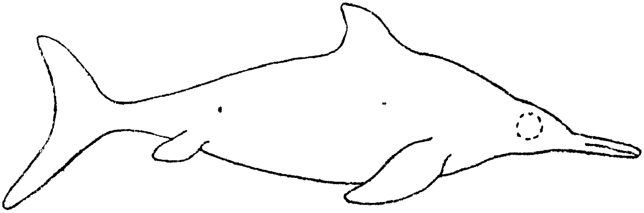
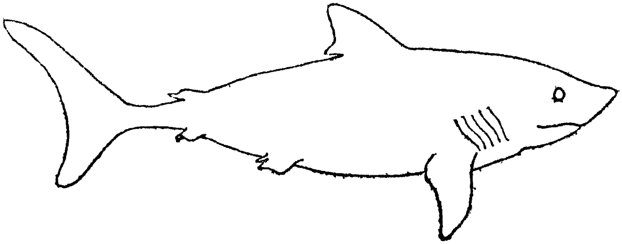


Fig. 2.—Above : outline of an Ichthyosaur, an extinct aquatic reptile. Below : outline of a shark. In both animals the tail fin is vertical. Note the gill slits of the shark.



The skull, too, has had its share of remodelling. The snout is long and gently tapering, but the roofing bones of the brain case have been reshaped exactly as though the resistance of the water had pushed them back from in front, so that the skull appears to be all front and back and no middle. The details of the bones involved differ in the *Odontoceti* and *Mystacoceti*, but the result is similar, the attainment of a more streamlined form. Although this looks so like a direct effect of water pressure the characteristic shape is attained in the embryo before any such deforming force can act; it is determined by heredity and not by environment. This does not imply that in evolutionary history the telescoping may not·have begun as a direct result of external pressure. It is not uncommon for a condition which could be brought about by external factors to be hereditarily determined. For this to be so may be of considerable survival value, for it constitutes a form of pre-adaptation; the individual is fitted to meet certain contingencies before they actually arise. In the present case, if the bones did slip extensively during post-natal life as a result of water pressure severe distortions of the brain would probably follow, with disastrous results; but if the whole skull can be genetically remodelled to the new adaptive shape then no disturbance of function need be involved.

Fig. 1 illustrates these modifications in the whale skeleton, with the skeleton of a dog for comparison. Such striking changes are possible only because the whales are completely aquatic and never need come ashore. This has meant that they can afford to have the body completely adapted for swimming, without the reserve that some ability to walk on land must be retained. A stranded whale is, in fact, quite helpless. This independence of the land has affected other functions besides locomotion. Hair is useless as a heat-retaining jacket to a totally aquatic animal, and in the whales the thick blubber takes its place as an insulator. This, as well as being a most effective method of conserving heat, also makes for better streamlining. Fig. 2 shows the outline of a fish and of an Ichthyosaur, for comparison with the whale in Fig. 1. The remarkable similarity is a reflection of the fact that all three groups are (or were) efficient swimmers, and streamlining in all attains a high degree of perfection.

Respiration. Since whales find their food under water.

and since submerged swimming is so much the more economical, they must be able to remain below the surface for considerable periods, and come up only at intervals for air. Some device for closing the nostrils so that water is not forced into the respiratory passages in deep diving is desirable, and the nostrils must be in a position such that they can easily be brought clear of the water. In both groups the nostrils are dorsal, and there are closing devices which are a combination of muscles and valvular flaps differing in detail, but fulfilling the same function and closing more firmly the greater the external pressure.

There is still some dispute about the length of time whales do or can remain submerged. The smaller *Odontoceti*, such as dolphins and porpoises, can stay submerged for about 10–15 minutes. The larger whales in normal feeding seem to remain below about the same length of time, but when pursued are capable of staying submerged for much longer. The bottlenose and the sperm whale hold the record, and are able to make dives lasting at least 30 minutes. How have whales succeeded in increasing their diving-time so much? Unfortunately they are inconvenient animals for physiological work, and therefore the only experiments that have been carried out concern the smaller species, porpoises, and even these are not easy to deal with. Since experimental data are so scanty and so difficult to obtain, rather roundabout calculations must be resorted to, and the conclusions drawn are therefore only tentative.

The first approach to the diving problem is to find out how much oxygen the whale needs, and how much it can take down with it when it submerges. It can carry oxygen in three ways, in its lungs, combined with the hæmoglobin in its blood, and combined with its muscle hæmoglobin. The lungs of the whales are not proportionally larger than those of land mammals, but there are certain differences in their mode of action. The rhythmical filling and emptying of the lungs in normal respiration is controlled by the brain. In land mammals this part of the brain is very sensitive to changes in the carbon-dioxide concentration in its blood-supply. Any increase in activity of the animal causes an increase in carbon-dioxide production, and the respiratory centre in the brain promptly responds by bringing about an increase in rate of respiration. The blood traversing the lungs is thus provided with more oxygen, and at the same time the extra carbon dioxide is blown off. When the carbon-dioxide level returns to normal so does the respiratory rate. It is accumulation of carbon dioxide acting on our brains, not actual shortage of oxygen, that makes it impossible for us to hold our breath for more than about a minute. In the whales this sensitivity to carbon dioxide has been lost, and there is therefore no stimulus to take another breath as soon as carbon dioxide starts to accumulate. Nevertheless, the oxygen demands of the animal have to be met, and we return to the lungs to see what further differences from those of land mammals are to be found. In man normally only a fraction, about 25 per cent, of the air in the lungs is renewed at each breath, and only about 4 per cent of the oxygen in the air is removed in the lungs. In the porpoise not only is 80 per cent of the air in the lungs renewed at each breath, but the percentage of oxygen removed from it also reaches the high value of 8–12 per cent. When diving probably even more of the oxygen is removed, since the air then stays in the lungs for a longer time. So far the whale appears to have more efficient lungs than we have, but the other side of the picture is shown when we consider not normal but maximal performance. By breathing more deeply and more rapidly a man can increase his rate of oxygen uptake to ten times the value it is when he is resting, but the porpoise can achieve at most only a three-fold increase. In other words, the terrestrial mammal is normally not using its lungs fully, but the porpoise is—most of its reserves have been brought into action permanently in order to secure the maximum amount of oxygen per breath.

The porpoise's blood has nothing unexpected about it; it can carry the usual 20 cc. of oxygen per 100 cc. of blood, and its volume in relation to body size is normal or at most only slightly greater than the usual for a mammal.

The muscles are unusually rich in hæmoglobin, and can carry 4·7 cc. of oxygen per 100 gm. of muscle, about six times as much as dog's heart-muscle does.

The particular porpoise on which these measurements were made weighed 170 kg. ; it took 10 litres of air into its lungs at a breath, and used 1 litre of oxygen per minute at the surface. (This is 6 cc. of oxygen per kg. body-weight per minute, which is surprisingly high. A man uses only 4·3 cc./kg./min., but the porpoise may well have been rather agitated during the experiment.) We now have enough information to draw up a balance-sheet for the animal, Its lungs contain 10,000 cc. of air of which 21 per cent is oxygen, giving 2,100 cc. Assuming the blood to be 10 per cent of the body-weight (possibly a bit over-generous), it could carry 3,400 cc. of oxygen. Assuming the muscles to be 40 per cent of the body-weight, they could hold another 3,200 cc., making a total of 8,700 cc. of oxygen in all. This is enough to last the animal only for about 8½ minutes, and it can stay down for about twice that length of time. How it does so is not yet fully clear. Muscles can work for a considerable time without oxygen and make up for it by consuming the extra later; but the central nervous system cannot do this and must have a constant supply. If the animal could have a priority rationing scheme for its oxygen and keep the central nervous system well supplied while the muscles went short, then its problem would be solved. This is exactly what is done in another group of aquatic mammals, the seals. When a seal dives the blood-supply to the muscles is cut off and only essential organs are supplied. It is not yet clear whether the same thing happens in the whales, and further experiments are necessary.

Data for the larger whales which can remain submerged for so much longer are very scanty, but Laurie gives some measurements for a 90-foot long blue whale. At first sight it might appear that if the proportions of lungs, blood and muscles remain unchanged then a larger whale should not be able to stay down any longer than a porpoise can. This is not true, for once again the factor of the smaller relative surface of the large animal enters into the calculations. A mammal loses heat mainly through its skin, so the smaller the animal the more rapidly it will cool and the more energy must it produce to keep itself warm. To keep at the same temperature, therefore, a large animal needs a much smaller basal metabolic rate than a small one. We have no direct measurements of the metabolic rates of large whales, but we do know that an elephant has a metabolic rate of something between a third and a half that of man. On the basis of relative surface areas, Laurie's blue whale would have a basal metabolism of less than a tenth that of a man, and he estimated its oxygen consumption as 36 litres per minute. Its lungs carry 640 litres of oxygen, and Barcroft estimated that its blood would carry 1,700 litres. Together this gives sufficient oxygen to last for 65 minutes of basal metabolism. So far we have made no allowance for any extra expenditure of energy by the muscles in swimming, nor have we taken into account the oxygen stored in the muscles. Laurie gives 56,000 kg. as the weight of the animal's muscles which, if it contains the same concentration of hæmoglobin as porpoise muscle, would carry

2,600 litres of oxygen. This weight of muscle would have a basal oxygen consumption of 17 litres per minute, and the 17 horse-power which Barcroft gives as necessary to propel his whale at 5 knots would require a further 85 litres per minute. The oxygen stored in the muscles would therefore last for about 25 minutes at 5 knots, and for a much shorter time at higher speeds. Presumably the muscle must be able to go on working for some time after it has used up its oxygen store, and repay its oxygen debt later just as happens in the seals. The very high concentration of hæmoglobin in the muscles does, however, seem to be sufficient to be of some value as an oxygen store, and it is interesting to note that the best divers, the bottlenose and the sperm whale, have also the muscles richest in hæmoglobin. In land mammals the amount of oxygen carried by the muscles is sufficient to last only for a matter of seconds, and serves as a short-term store between one contraction and the next, and the ability to act as a long-term store is something peculiar to diving animals.

Whales not only make long dives, but they also dive deeply. Exact measurements are difficult to make, but there is general agreement that 100 metres is well within their powers. At this depth the pressure will be eleven times as great as at the surface. A human diver, if he comes up rapidly from this depth, will suffer from caisson sickness (bends), but the whale shows no evidence of similar trouble. When subjected to increased pressure the blood takes up more nitrogen than at air pressure, eleven times as much at eleven atmospheres. The diver's caisson sickness is caused by the sudden release of pressure, which allows the extra nitrogen to bubble off more rapidly than it can be got rid of at the lungs. The bubbles may be large enough to cause stoppages in the circulation, and if such a stoppage occurs in the blood-vessels supplying the central nervous system, death or paralysis may result. The diver avoids this by being decompressed gradually, but the whale cannot afford to come up very slowly, and its immunity to caisson sickness was something of a mystery for some time. There is really no mystery, for the comparison between the whale and the diver is not a valid one; the whale is not constantly supplied with air at eleven atmospheres pressure as a diver at 100 metres depth would be, but goes down with only a limited supply of air, and can therefore take up only as much nitrogen as is contained in one filling of the lungs. Its problem on coming up will then not be very acute, and it may be able to get rid of its excess nitrogen without bubble formation. The blood supplied to the central nervous system passes on its way through a series of networks of fine vessels whose function is still imperfectly understood. They have been thought to act as a store of extra blood and hence extra oxygen for the brain during a dive, but are almost certainly too small for this to be their principal function. They could, however, very well act as bubble traps, and if any bubbles are formed prevent them reaching the blood-vessels of the central nervous system, the only place where their effects would be really serious. The blockage of a few of the small vessels in the network would be of no consequence, as plenty of other channels would remain free and the blood would continue through these to supply the nervous system. The blockage would, of course, be only temporary, since on returning to the surface the excess nitrogen would be gradually got rid of through the lungs and the bubbles would then redissolve. In connection with depth of diving it is of some interest that the lungs of the best divers are relatively small; in the bottlenose the weight of the lungs is only ·9 per cent of the body-weight, compared with 1·2 per cent in the blue whale and 1·4 per cent in man. This may be partly because any gain in the amount of oxygen taken down is more than counterbalanced by the extra buoyancy to be overcome, but it also has the advantage of reducing the amount of nitrogen taken down and hence decreasing the danger of caisson sickness on returning to the surface.

Water Balance. Water balance also presents a problem for a marine mammal, just as it does for the shipwrecked sailor on a raft. Land mammals usually have some source of drinking water, and often, too, eat juicy food which itself supplies much of the necessary fluid. A source of water is necessary because there is a continual loss by evaporation from the skin, in the breath and in the urine. The losses must be made good or the animal will dry up. The whale does not lose so much water as a land mammal, for there can be no sweating, but the fluid lost in breath and urine must be replaced. The only sources available are the food and sea water. A whale's body fluids are only slightly more concentrated than those of land mammals, nothing like as concentrated as sea water, so that drinking alone cannot solve the problem. In order to use sea water the extra salts must somehow be eliminated, or drinking will only result in making the body fluids more salty, and this would be fatal to the animal. The krill cannot supply extra water, since its body fluid is just about the same concentration as sea water. Fish, however, have body fluids more dilute than sea water, and therefore the fish-eaters have a less acute problem than the whalebone whales. The simplest way out of the impasse is to get rid of the extra salts through the kidney by producing a urine which is much more concentrated than the body fluids. This entails a considerable amount of work, and demands a very efficient kidney. Unfortunately we do not possess sufficient information to draw up a water balance-sheet for the animal and see whether the kidneys are indeed responsible for getting rid of all the salt, or whether some other auxiliary elimination goes on elsewhere. The kidneys of whales are, however, very large, and it seems likely that they are capable of performing the necessary work. Further experiments alone can settle the question.

Reproduction. Reproduction always presents a problem when drastic changes of habitat are made. The amphibia were the first vertebrates to come on land, and they are still not wholly independent of the water, for they must return to it to breed, and the young pass their early life there. The reptiles solved the problem of reproduction on land by laying large eggs protected by a shell and containing sufficient food for the young to develop before hatching to a stage in which they are capable of looking after themselves. The mammals protect the eggs by retaining them inside the body of the mother, and this allows her also to provide the developing embryos with food as they grow until they have reached a large size. Even after birth the mother provides the young with nourishment in the form of milk until they are able to make their own way in the world. Having achieved this method of reproduction, suited to land life, a return to the water presents difficulties. The whales are the only living secondarily aquatic vertebrates which reproduce away from land. Turtles come ashore to lay their eggs; seals do the same for breeding, and the young are not able to swim immediately but remain on shore for some time. In the whales, however, the whole process is carried out at sea. The young must of necessity be born sufficiently advanced to be able to swim right from the start. The period of gestation is therefore long, and the litter number is reduced, one calf at a time being usual. The same reduction in the number and advanced stage at birth are found also in those land mammals whose young are unprotected. The horse is a familiar example, and the contrast between the young hare, born in the open form, and the baby rabbit born in the protection of the burrow, is striking. The leveret has its fur, and is able to run soon after birth, while the rabbit is born naked, blind and helpless.

The actual birth of the young presents no special difficulties for an aquatic mammal, since the first breath is not drawn until the process is completed, but suckling at sea does require some special provisions. The mammary glands of the whales are provided with reservoirs in which the milk accumulates; the muscles of the glands are unusually large and by their contraction the milk is forced down the throat of the calf very rapidly, so that feeding occupies only a short time.

The young of the humpback, sperm whale and sei whale are about 14 feet long at birth, those of the fin whale and blue whale are 20 feet long; they are weaned at five to six months. By this time they have doubled their length, which implies something of the order of an eight-fold weight increase. This rapid growth is correlated with a very concentrated food; whale milk contains 10 per cent of protein, and its fat content, too, is very high. The human baby has only doubled its weight in six months, but this is on the basis of a milk which contains only 1·6 per cent protein.

Young mammals are less able to withstand extremes of heat or of cold than are adults, and whales migrate to temperate waters for breeding. The humpback, blue and fin whales are largely south polar species, but in the breeding season they move north to warmer waters. The young are not exposed to extreme cold until they have had time to lay down an adequate insulating layer of blubber: the high fat content of the mother's milk allows them to do this very quickly.

After weaning growth continues to be rapid, and the whales are sexually mature by their third year. The maximum length of life is not known, but the humpback lives at least eighteen and the sei whale at least fifteen years. Since the gestation period is long, eleven months for the humpback, twelve for the sei, and sixteen for the sperm whale, the females cannot breed more often than once in two years, and will rarely produce more than a single young at a birth. This means that the replacement rate of the population is low, and depletion by over-fishing is therefore a very real danger. Whaling is limited by international agreements * which restrict the length of the season and the areas in which catching is permitted, and prohibit the taking of whales under sizes agreed upon for each species. In spite of these limitations an analysis of the figures for the catch of the 1938–9 season shows that over-fishing was taking place. The six years of the war have no doubt allowed some recovery to happen, but if the use of radar makes hunting much more efficient, then more stringent limitations will have to be made or some of the whales will be in danger of extinction.

The whaling industry is well aware of this risk, and new regulations are constantly being made in accordance with what the analysis of each year's catch shows to be desirable. This season a new form of restriction is being tried; the total catch is to be limited. For this purpose the different species caught must all be taken into account. This is done by reducing them all to 'blue whale units'; 1 blue whale = 2 fin = 2½ humpback = 6 sei whales. This year the figure decided upon for the total catch is 16,000 blue-whale units. Quite apart from the economic undesirability of killing the goose that lays the golden egg, no biologist could view the prospect of over-fishing of the whales with anything but dismay. They are one of the most interesting groups of mammals, and their extinction would be a zoological tragedy.

Although there remain many things about whales which we do not understand, we yet know sufficient of their anatomy and physiology to be amazed at how completely

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* The Japanese did not see fit to participate in these agreements before the war.

adapted they have become to their unorthodox environment, and at the same time have done so without anything essentially different from what is the rule in their terrestrial relatives. Their bones have altered shape, some have been lost, but their skeletons are built out of the same bricks as our own; their blood is the same, their muscles are no more powerful, they have not grown an extra pair of lungs: and yet, by an integration of small alterations, one here, another there, none sufficiently drastic to upset the harmonious functioning of the whole, they have achieved complete mastery of their new environment.

FURTHER READING

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Ommanney, F. D. (1938). *South Latitude.* London, Longmans. (Whaling at South Georgia. Exciting and written for popular consumption.)

Scoresby, W. (1820). *An Account of the Arctic Regions.* Edinburgh. (Full of good stuff about old-time whaling.)

Howell, A. B. (1930). *Aquatic Mammals.* Springfield, Ill. C. C. Thomas. (Anatomy, but hardly any physiology, of all aquatic mammals. Too difficult without some previous knowledge.)

Barcroft, J. (1938). Chapter V in *Features in the Architecture of Physiological Function.* Cambridge University Press.
(Important, but not comprehensible to the layman.)

Several of the *Discovery* Reports contain interesting material on whales.

THE CHEMICAL BASIS OF COMPETITION BETWEEN MICROORGANISMS

By P. W. Brian

FEW scientific discoveries have appealed to the public imagination to the same extent as that of penicillin. This is not really surprising when one considers the dramatic rapidity with which the drug will deal with serious infections that would otherwise be almost certain to end in death, and the fact that the drug was discovered, and actually produced on a commercial scale, during wartime when such severe infections are particularly abundant. Penicillin has saved tens of thousands of lives in the few years that have elapsed since its discovery; one result of its great importance to medicine has been to some extent to obscure the biological context of its discovery. In fact, the isolation of penicillin depended on previous biological observations every bit as much as the manufacture of the atom-bomb depended on a century of physical research. Its unique therapeutic properties have overshadowed the fact that it is but one of a general class of substances produced by microorganisms, all probably having a considerable part to play in maintaining the balance of nature. It is now known that many microorganisms, belonging to widely differing groups—bacteria, fungi (moulds and toadstools), actinomycetes (a group in many ways intermediate between bacteria and fungi) and green algæ (the simplest green plants, frequently unicellular or filamentous)—produce and excrete into the substratum on which they are living chemical substances inimical to the growth of other microorganisms of the same or different groups. It is hoped in this article to give a more general account of the biological background of the production of these 'antibiotic substances,' as they are called, but since penicillin has attracted such general public attention it provides a good starting-point. An account of how penicillin was discovered, and how it is produced and what it will do can suitably be used to give a general idea of how other substances of the same general nature may be studied. It is for this reason only that the story of penicillin, which has now often been told, is given prominence here.

In 1929, Fleming was working at St. Mary's Hospital, London, on *Staphylococcus aureus,* the bacterium responsible for boils and certain bone diseases. In the course of this work he was growing *Staphylococcus* on a nutrient jelly in a glass dish. Under such conditions the organism appears as numerous yellowish specks ('colonies') which, in mass, give a cloudy appearance to the clear jelly. Fleming had occasion to lift the lid of one of these dishes to examine the colonies of *Staphylococcus* more closely and a mould spore fell into the dish. This kind of accident happens frequently in bacteriological and mycological laboratories, as the air around us almost always contains great numbers of bacteria, mould spores and other microorganisms. The mould spore germinated and produced a small circular colony, green with a white edge. Fleming made the observation that the small bacterial colonies close to the mould colony were being 'lysed' (dissolved). He followed this acute observation by growing this mould in pure culture on a liquid nutrient solution, on which it developed as a corrugated felt on the surface of the liquid, at first white but soon turning green, and found that after several days' growth the liquid nutrient solution beneath the mould felt had acquired marked disinfectant properties.

He examined the properties of this 'culture filtrate' in some detail and found that it would inhibit the growth of certain bacteria, including many pathogenic ones, at very low dilutions; other bacteria, on the other hand, were not affected. Fleming also showed that the production of this inhibiting substance, which he called penicillin, did not appear to render the culture solution any more toxic to warm-blooded animals. But he was unable to extract the penicillin from the culture filtrate and it remained a laboratory curiosity for some years.

The green mould that was concerned in these observations is one known as *Penicillium notatum*, closely related to those green moulds commonly seen growing on old leather or foodstuffs. The nutrient medium on which Fleming grew it to produce his penicillin containing culture filtrates was a complex organic broth made from meat and peptone (a partially digested extract of meat, casein or yeast). Other workers subsequently (1932) showed that penicillin was also produced by this mould on synthetic media of known composition, consisting of a sugar (glucose or cane-sugar) with a few simple mineral salts—sodium nitrate, potassium phosphate, potassium chloride, magnesium sulphate and a little iron sulphate. They also showed that penicillin was very unstable chemically, and were unable to devise methods of concentrating the culture filtrate without destroying the penicillin, still less of isolating the penicillin itself.

The first great contribution of Florey and his associates at Oxford was to discover a method whereby the penicillin could be obtained from the culture filtrate in a highly concentrated form, as a dry powder. One of the difficulties, in an investigation of this kind, is to know whether by a certain chemical or physical treatment you have destroyed the substance you are working on, or to determine the proportions in which the substance is divided between the various products of a fractionation procedure. For example, Florey and his colleagues required to know the effect of treatment of a culture filtrate with an organic solvent, whether the penicillin had been destroyed, whether it had passed into the organic solvent or whether it had remained in the aqueous culture filtrate. In chemical work with known substances, analytical methods can usually be devised which will give the answer to questions of this type in a few minutes, when a further process of concentration and purification may be embarked upon. In the case of such a substance as penicillin at this stage of the research its only known property was its antibacterial effect, and the only possible method of tracing the material in an experimental fractionation procedure is by estimation of the antibacterial activity of the various fractions. At the best of times a biological assay (i.e. a quantitative estimation based on a biological response) of this type is slow and cumbersome as compared with a chemical analysis. The slowness may be a great disadvantage where an unstable compound such as penicillin is being studied. The Oxford workers were greatly helped by a fairly simple but effective method of biological assay devised by Heatley. Essentially this was carried out as follows. A flat dish of nutrient agar jelly is uniformly inoculated with *Staphylococcus aureus*. A small glass tube, open at both ends, is placed firmly on the agar and a small quantity of the penicillin-containing solution to be assayed is poured in, and the dish incubated. The penicillin diffuses outwards from the glass tube and inhibits the growth of the *Staphylococcus* where it is present in sufficient concentration, so that the effect produced is a clear circular halo around the glass tube surrounded by an opaque background where the bacterial colonies have developed. The diameter of the halo is proportional to the concentration of penicillin in the fluid put into the tube. The general principle of this method of assay has not been improved upon and has been a most valuable tool in the development of methods of isolating penicillin from *Penicillium notatum* culture filtrates.

It is not proposed here to go into detail concerning the methods of extraction and purification of penicillin developed at Oxford, or the refinements subsequently developed, but an indication of the kinds of difficulty encountered and the methods adopted to overcome these will be given. Earlier workers had found that penicillin could be extracted from the culture filtrate into certain organic solvents (such as ether or amyl acetate) if the culture filtrates were first acidified. Penicillin decomposes rapidly under acid conditions, and the process of extraction must be completed rapidly after acidification. It was hoped that when the ether extract was evaporated penicillin would be left, but the free acid penicillin is too unstable to stand this treatment. (Penicillin is an organic acid, the free acid being less stable than its salts.) The Oxford workers made the important discovery that the penicillin could be taken back into a smaller volume of water by shaking very dilute alkali with the ether or amyl acetate extract. By alternate acidification and extraction into an organic solvent and re-extraction into dilute alkali, using progressively smaller volumes of fluid, a concentrated aqueous solution of penicillin could be obtained, all the operations being carried out in the cold. This concentrated aqueous penicillin solution was then frozen in solid carbon dioxide ('dry ice') and the water (or rather ice) removed by application of a high vacuum. By this 'freeze-drying' technique, Florey and his colleagues were successful in obtaining a yellowish brown powder of very high antibacterial activity which they thought was almost pure penicillin, though it was subsequently found to be only 5-10 per cent pure.

Apart from the great difficulties arising out of the instability of penicillin the Oxford workers were much hampered by the great volumes of culture filtrate required to produce very small quantities of penicillin. They found it essential to grow the mould on shallow layers of culture medium, about 1 cm. in depth; if deeper layers were used lower penicillin concentrations were obtained and the increased volume of culture filtrate did not compensate for the reduced penicillin concentration. As soon as they had demonstrated the remarkable therapeutic properties of penicillin and its production on a larger scale became a matter of urgent practical importance, ways and means of increasing the yield were sought. Three main advances have since been made in this field, all of them by American workers.

In the first place much greater yields of penicillin were obtained by a simple modification of the culture medium used for growth of the mould. Moyer found that by addition of 5–10 per cent of corn-steep liquor to the sugar-mineral salt medium, yields of penicillin might be increased five-fold. Corn-steep liquor is a by-product of starch manufacture; it is a complex mixture containing carbohydrates, proteins and degradation products of proteins and many other substances in small quantities. It has long been used in the fermentation industries. The mechanism by which it increases penicillin yield is at present unknown.

A second improvement was the discovery of strains of *P. notatum* with a greater capacity for penicillin production. All the research work up to the first production of penicillin by Florey and colleagues was carried out with sub-cultures descended from Fleming's original mould. This was at first considered to be unique. It was subsequently found that most strains of a whole group of slightly varying green moulds, common in all cultivated soils, known to mycologists under the group name of '*Penicillium chrysogenum* series', were penicillin-producers. Examination of many strains at the North Regional Research Laboratory of the United States Department of Agriculture led to the discovery of two strains (NRRL 1249 and NRRL 832), which are today in use in penicillin factories all over the world. Many strains, on the other hand, produced penicillin in small quantities, and some produced none at all. Strain specificity of this type, where one has different strains similar morphologically but differing in metabolism, is a phenomenon observed in the production of most antibiotic substances, and, indeed, in all the chemical activities of micro-organisms.

These two improvements, of the medium and of the mould, meant that culture filtrates could be obtained containing approximately 100 Oxford units of penicillin per litre (an Oxford unit is an arbitrarily defined measure of penicillin activity) where concentration of only 5 Oxford units could be obtained before.

A third improvement was in the way the mould is grown. Florey and all earlier workers had grown the mould on flat layers of medium in bottles, flasks, or trays. The mould then develops as a felt on the surface of the medium and the productive surface is limited. Further, the ratio of volume of medium to surface cannot be increased beyond a certain point, approximately where the depth of medium is 1 or 2 cm. It is obvious that the use of such a system as this on a large scale is very greedy of space and involves much handling of separate culture vessels. In commercial production this method is now almost completely superseded by stirred deep cultures. In this method the mould is grown in large reaction vessels, holding hundreds of gallons of culture medium which is kept constantly stirred and supplied with sterile air. Under these conditions the mould develops as numerous small pellets, evenly distributed throughout the medium. The mould surface producing penicillin is much increased, and the peak of penicillin production is reached several days sooner than in still-surface cultures. The advantages of this method are obvious; once the difficulties of stirring and aerating without introducing con-

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Plate 1.—*R. rattus* on the run. (Note the large ears, long tail and that this specimen is not black.)

Plate 2.—*R. norvegicus.* (Small ears and relatively short, thick tail. The lengths of drain piping have been put by a well-worn rat run, and contain bait.)

(Photo by H N Southern, Bureau of Animal Population)

Plate 3.—A characteristic sight in a rat-infested warehouse. (Beans spilt on the floor and sacks collapsing.)

Plate 4.—Flaked rice and cheese attacked by rats and mice. (Rat droppings can be seen on the rice.)

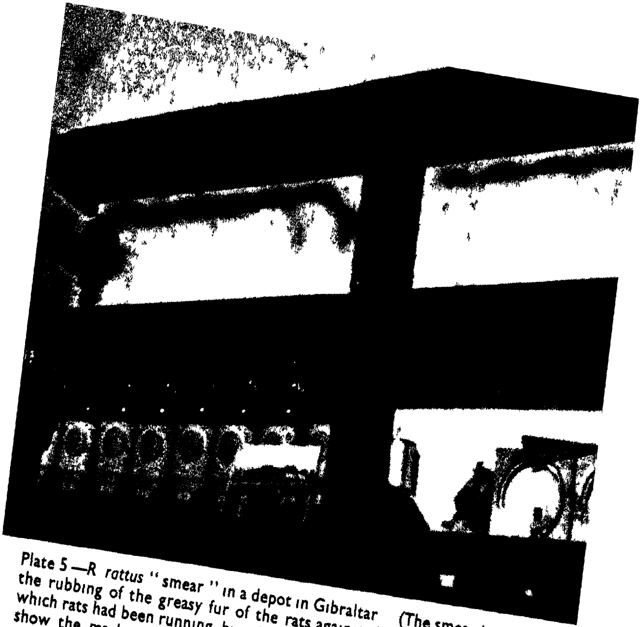
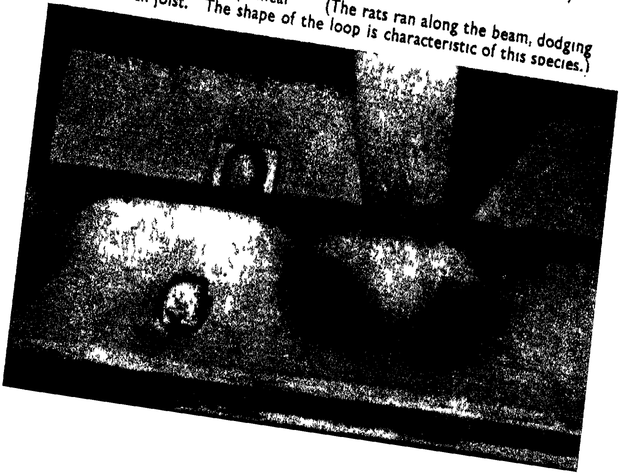


Plate 5.—*R. rattus* "smear" in a depot in Gibraltar. (The smear is due to the rubbing of the greasy fur of the rats against the wall. Bottles, over which rats had been running, have been removed from the middle shelf to show the marks. *R. norvegicus* makes smear too, and so do mice.)

Plate 6.—*R. rattus* "loop smear." (The rats ran along the beam, dodging under each joist. The shape of the loop is characteristic of this species.)



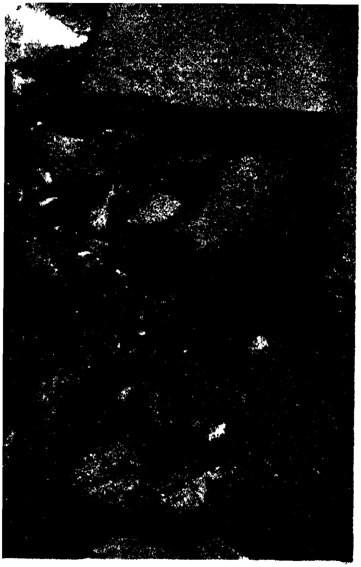


Plate 7—*R norvegicus* burrow under a London pavement. (The rats here may have been feeding in the sewers)

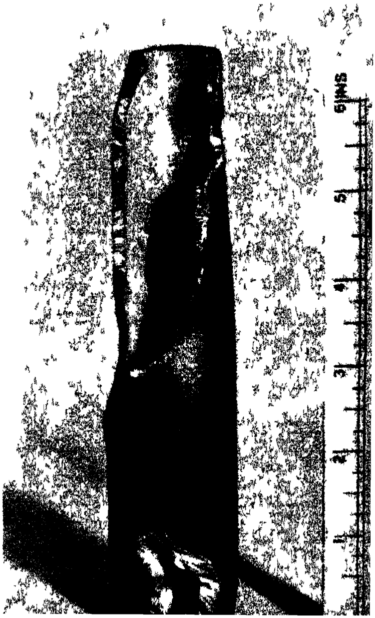


Plate 8—Damage by gnawing to a lead pipe (The owner of the pipe reported that this was 48 hours' work by one *R norvegicus*, which had been accidentally locked in a cupboard through which the pipe ran The plumber took away part of the damaged length This apparently pointless gnawing by rodents has the function of preventing the incisor teeth from growing too long Like our finger-nails, they grow throughout life.)

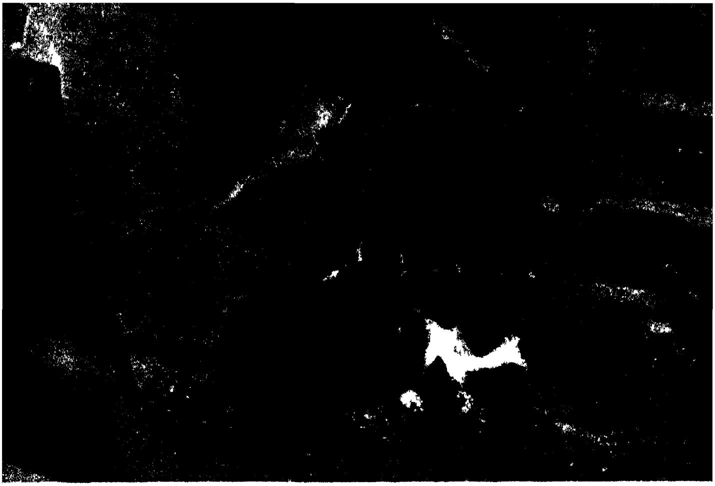


Plate 9.—Prebaiting. (Five *R norvegicus* feeding at a heap of harmless bait.)

Plate 10.—The kill

Plate 11.—Baiting a manhole during the London sewer rat campaign. (A sewerman is lowering bait down the shaft in a depositor which makes possible baiting in the inspection chamber without going down.)

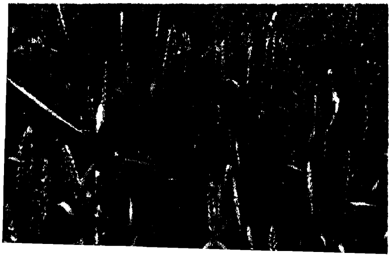
Plate 12.—A sewer bait tray in position. (Trays like this are put in when there is no shelf, or benching, for the bait. After an interval, while they become accustomed to the new object, rats readily use the rope to reach the tray.)

(Plates 3–12 inclusive are Crown Copyright reserved.)

Plate 13.—Spraying with sulphuric acid. Corn buttercup in winter wheat. Left : sprayed—buttercup destroyed. Right : Unsprayed.

(Photo courtesy of Imperial Chemical Industries Limited)

Plate 14—(*a*) Weedy wheat crop, untreated.



(*b*) Wheat crop similar to (*a*) after treatment with calcium cyanamide.

(Photos courtesy of Messrs. Shaw, Scott and Co.)

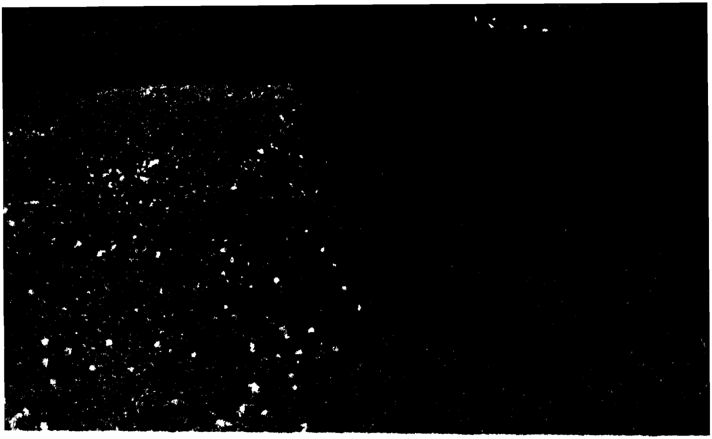


Plate 15.—Effect of Sodinoc and D.N.O.C. (right) in reducing charlock when applied early, compared with unsprayed area (left).

(Photo courtesy of the Director, Rothamsted Experimental Station.)

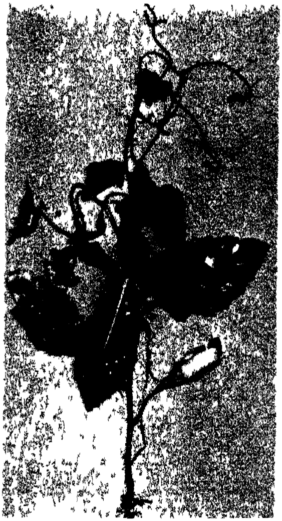


Plate 16.—Charlock sprayed with C.L.C. (Methoxone), showing distortion of the stems and destruction of the flowers.

(Photo courtesy of the Director, Rothamsted Experimental Station.)

Plate 17.—Successful treatment of wheat crop with Agroxone to destroy charlock. Left : treated ; right : untreated.

(Photo courtesy of Plant Protection Limited.)

taminating organisms were overcome, it is clear that the saving in space and handling-time is immense and that this method of growing the mould makes penicillin production almost completely comparable with other chemical production processes.

As it is not proposed in this article to stress the medical implications of antibiotic substances, only a brief outline will be given of the pharmacological properties of penicillin. The first feature of the antibiotic activity of penicillin is its *selectivity*. It is not toxic to the mould that produces it, nor to other fungi. Some bacteria and some of the closely related group actinomycetes are extremely sensitive to penicillin, others are relatively insensitive. This is clearly shown in the table below of results obtained by the

Bacterial species	*Disease caused*	*Dilution at which growth was inhibited*
		1 part in :—
Neisseria gonorrhœa	Gonorrhœa	2,000,000
Staphylococcus aureus	Boils, carbuncles, osteomyelitis, etc.	1,000,000
Streptococcus pyogenes	Scarlet fever, septicæmia	1,000,000
Bacillus anthracis	Anthrax	1,000,000
Actinomyces bovis	Actinomycosis ('woody tongue')	1,000,000
Pneumococcus	Pneumonia	250,000
Salmonella typhi	Typhoid	10,000
Proteus	Mainly non-pathogenic, but present in some wound infections	4,000
Pasteurella pestis	Bubonic plague	1,000
Vibrio choleræ	Cholera	< 1,000
Escherichia coli	Mainly non-pathogenic	< 1,000
Pseudomonas pyocyanea	'Blue pus' in infected wounds	< 1,000
Mycobacterium tuberculosis	Tuberculosis	< 1,000

of the organism producing a new substance and the development of methods of extracting and purifying the active material. This search is undoubtedly being undertaken largely in the hope of finding a substance capable of use in medicine for treatment of those conditions, such as tuberculosis or typhoid, which are not susceptible to penicillin treatment. Very few indications of success in this search have been obtained, but many new antibiotic substances have been described with very interesting biological and chemical properties.

Three main groups of microorganisms have been found to produce antibiotic substances—fungi, bacteria and actinomycetes. An example is also known of the production of an antibacterial substance by a unicellular green alga—*Chlorella vulgaris*. Among the fungi the property is particularly widespread among the group, commonly recognised as 'moulds,' known as the fungi imperfecti, among the toadstools (basidiomycetes) * and to a lesser extent among the ascomycetes. The lower filamentous fungi—phycomycetes—do not appear to produce antibiotics. Among the bacteria, a group of spore-forming bacilli—the *Bacillus subtilis—mesentericus—mycoides* group and the non-sporing *Pseudomonas aeruginosa—fluorescens* group—are particularly notable producers of antibiotics. Many actinomycetes have antibiotic properties.

The antibiotic substances produced by these microorganisms vary considerably in their biological properties. Some are remarkably specific, others are of general toxicity. A few examples will illustrate this point.

PENICILLIN. This, as we have seen, is produced by a mould (*Penicillium notatum*) and is very active against some bacteria but inactive against others. It is non-toxic to fungi; it is toxic to some actinomycetes. It is of low toxicity to warm-blooded animals. Penicillin is, therefore, of high specificity.

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* The reader may wonder why such large organisms as the toadstools are included as *micro*organisms. Many basidiomycetes are microscopic, and the vegetative stage of even the largest toadstools is composed of fine strands of hyphæ ramifying through the soil.

PATULIN is produced by *Penicillium patulum*, a green mould superficially not unlike *P. notatum*. It is moderately toxic to all bacteria and fungi, and is too toxic to mammals to be administered internally. Patulin is a good example of a non-specific antibiotic substance.

GLIOTOXIN, produced by the mould, *Aspergillus fumigatus* and *Trichoderma viride*, among others, is quite highly active against a wide variety of bacteria, fungi and actinomycetes, and is also extremely toxic to mammals. It is another example of a non-specific antibiotic.

VIRIDIN is also produced by the mould *Trichoderma viride*. It is not antibacterial, is exceedingly active against certain fungi but only moderately active against others. This substance is, like penicillin, highly specific, but with quite a different range of activity.

GRAMICIDIN is produced by *Bacillus brevis* (a spore-former common in soil). It has much the same sort of 'antibacterial spectrum' as penicillin, is not toxic to fungi, but is much more toxic than penicillin to warm-blooded animals.

STREPTOMYCIN is produced by *Actinomyces griseus* and is of fairly general antibacterial activity. It is not toxic to moulds and is of only moderate toxicity to warm-blooded animals. This substance shows some specificity and is, in fact, the only antibiotic other than penicillin showing much promise of finding clinical applications.

Antibiotic substances are of widely differing chemical types. To exemplify this we may consider those antibiotics whose biological properties have just been discussed. PENICILLIN behaves as an organic acid, forming salts and esters. Its molecule contains carbon, hydrogen, oxygen and nitrogen. It is stable in neutral solution but very unstable in acid solutions. PATULIN is a fairly simple substance, of known molecular structure, of empirical formula $C_7H_6O_4$. It is quite stable. GLIOTOXIN is also of known structure, more complex than patulin and containing sulphur and nitrogen in its molecule. It has the empirical formula $C_{13}H_{14}N_2S_2O_4$; it is stable in acid solutions but unstable in neutral or alkaline solutions. VIRIDIN is of unknown structure, but its molecular formula is known to be $C_{20}H_{16}O_6$. Like gliotoxin it is stable in acid solutions but quickly destroyed in neutral or alkaline solutions. The four substances so far described are soluble in many common organic solvents, ether, benzene and chloroform, and also in water. GRAMICIDIN is chemically quite distinct from any of these; it is not soluble in water or any organic solvents except alcohol. It is a polypeptide, that is, a simple protein; it has a high molecular weight, its empirical formula being fairly close to $C_{74}H_{105}N_{15}O_{13}$. Not much is known of the chemistry of STREPTOMYCIN; it contains carbon, hydrogen, oxygen and nitrogen and behaves as an organic base. From these few examples we can see that antibiotics may be of widely different chemical types, varying from quite simple molecules such as that of patulin to complex protein-like substances such as gramicidin.

It was at one time thought that the production of a given antibiotic substance was characteristic of a given species of microorganism, but as more knowledge has been acquired this view has been considerably modified. It now appears that different strains within a species may vary widely in their antibiotic potentialities and that, on the other hand, widely differing species may produce the same antibiotic substance. A particularly good example of strain specificity is to be found in the mould *Trichoderma viride*, common in most soils. Many strains of this mould produce no antibiotic substance, some strains produce gliotoxin, which as we have already seen is antibacterial and antifungal; other strains, morphologically indistinguishable, produce viridin, which is active only against certain fungi. On the other hand, the same antibiotic may be produced by widely differing organisms. Patulin is a good example; it is produced by several species of the mould genus *Penicillium*, by *Aspergillus clavatus* and by a species of *Gymnoascus*. Gliotoxin is produced by species of the genera *Penicillium*, *Aspergillus* and *Trichoderma*, and penicillin-like substances are produced not only by various species falling into the *Penicillium chrysogenum* series but also by quite a number of distinct species of *Aspergillus*.

To add to the complexity of the situation, some organisms produce a mixture of antibiotics, or may produce different antibiotics under different circumstances. *Aspergillus fumigatus*, for instance, produces a mixture of gliotoxin, another highly antibacterial substance helvolic acid (also called fumigacin) and a weakly antibacterial pigment fumigatin. An even more complex example is provided by the bacterium *Pseudomonas pyocyanea*, which produces a weakly antibacterial violet pigment known as pyocyanine and five or six other substances, recently obtained in pure form, of varying degrees of antibacterial activity. An example of an organism producing different antibiotics under different circumstances is provided by certain strains of *Penicillium notatum*. Growing on the type of medium described earlier in this article, penicillin is produced. This type of medium, containing a nitrate as nitrogen source, becomes more alkaline as the mould grows; with media containing nitrogen as an ammonium salt the medium tends to become acid as the mould grows, and the culture filtrate is active not only against *Staphylococcus* but also against *Escherichia coli*, which is not sensitive to penicillin. The substance produced under these circumstances is known as notatin, and the pure material is of extraordinarily high antibacterial activity. Notatin is an enzyme, antibacterially active only in the presence of glucose, or a few other sugars, and air or oxygen. It is, in fact, an enzyme of the type called glucose-aerodehydrogenases, and it catalyses the oxidation, in the presence of oxygen, of glucose to gluconic acid with the simultaneous formation of hydrogen peroxide. It is the hydrogen peroxide formed which is responsible for the antibacterial activity.

Most of the antibiotics described are very minor products of metabolism. Yields of a few milligrams from each litre of culture filtrate are common, this being a very small fraction either of the weight of organism produced or of glucose (or other carbon source) broken down by the organism. As the term 'antibiotic substance' is usually employed it refers only to minor metabolic products of this type, which make up for low yield by high activity. Certain major metabolic products may also be inhibitory to other organisms if present in sufficient concentration. For instance, the mould *Aspergillus flavus*, if grown on a medium containing 15 per cent of sucrose, will convert one-third of the sucrose to kojic acid, subsequently breaking the kojic acid down to carbon dioxide. Kojic acid is a mild disinfectant, of the same order of activity as phenol; it will be seen that a culture filtrate produced by this mould, which may contain 5 per cent kojic acid, may have quite marked antibacterial properties. A reasonable conception of an antibiotic substance would include major metabolic products of low activity, such as kojic acid, and minor metabolic products of high activity, such as penicillin. There is in fact a continuous gradation between these two extremes, such substances as patulin, produced in moderate quantity and of moderate activity, falling midway between.

As a result of this survey of some of the properties of antibiotic substances we can see that the term 'antibiotic' is by no means accurate. By derivation it should refer to a substance antagonistic to life in general. Some of the products which we have considered have general toxicity (e.g. gliotoxin) and the term antibiotic may be considered to be suitable, but to describe a substance such as penicillin, which owes its great medical importance to being antagonistic only to certain kinds of living organisms, it is a most unsuitable term. However, its use has achieved general acceptance and will doubtless continue.

We have finally to consider the rôle of antibiotic substances in nature. It cannot be supposed that their significance begins and ends with their possible uses in human and veterinary medicine. To get an idea of their natural rôle one has to turn to their natural habitat. So far as it is possible to speak of a natural habitat for almost ubiquitous microorganisms, we may say that a very high proportion of those organisms known to produce antibiotic substances live normally in soil. The upper layers of almost all soils are very rich in microorganisms of many different kinds. In such a habitat the food-supply is restricted and it is obvious that if an organism can, by secretion of a substance toxic to other types of organisms, surround itself by a protected zone, it will be at an advantage. If one examines the microflora of a cultivated soil one finds that amongst the most common moulds are those known to produce penicillin, gliotoxin, viridin or patulin. Spore-forming bacteria of the type which produce gramicidin and other as yet unidentified antibiotics are common, as well as a great variety of antibiotic actinomycetes. It is clear that the balance between the various microorganisms in soil must be radically affected by the secretion of antibiotic substances.

This is not mere hypothesis. Plant pathologists have long known that there are organisms in normal soils antagonistic to certain soil-inhabiting plant-pathogenic fungi.

Henry, working in Canada on cereal root-rotting fungi, showed that if these fungi were grown in sterilised soil, and wheat seed sown in this inoculated soil, the seedlings produced suffered very severely from root-rot. If a pinch of normal prairie soil were added to the sterile soil inoculated with the pathogen, the severity of the root-rot was much reduced and the pathogenic organisms tended to decrease in numbers. This he attributed to antagonistic organisms present in the prairie soil. Weindling in 1932 demonstrated a similar state of affairs in Florida soils, working with the pathogenic fungi responsible for damping-off of citrus seedlings. He found that one organism present in soil particularly concerned with antagonism to the damping-off fungi was the green mould *Trichoderma.* He next showed, by growing *Trichoderma* and the damping-off fungi in association under close observation, that *Trichoderma* was able to kill the pathogens at a distance, as if by the production of a diffusable toxic material. He then found that if *Trichoderma* were grown on a liquid nutrient solution, the solution became highly toxic to the plant-pathogens with which he was concerned and, finally, he succeeded in isolating the toxic substance concerned, the substance now known as gliotoxin. This classical research demonstrated quite clearly that one of the factors restraining the development of certain plant pathogens in soil was the production of an antibiotic substance by the mould *Trichoderma.* Similarly, in Holland, Van Lujik obtained a *Penicillium* (*P. expansum*) from soil which was antagonistic to fungi causing damping-off of lucerne seedlings. He showed that this *Penicillium* produced a diffusible toxic substance, subsequently shown by Raistrick and his colleagues to be patulin.

Bearing these well-established cases in mind, we may proceed to consider the possible relation of antibiotic substances to broader problems of soil fertility. Soil is not merely a medium of suitable physical structure to hold the necessary nutrients for the growth of plants. If it were so, plant life would soon come to an end through shortage of essential nutrients. These are, in fact, to a considerable extent actually produced in the soil. One of the nutrients that all the higher plants need is a source of nitrogen. This must be supplied either as a nitrate or as an ammonium salt; green plants cannot utilise atmospheric nitrogen or nitrogen organically combined. Under what may be loosely termed natural circumstances, that is where artificial fertilisers are not applied to the soil, most of this ammonium or nitrate nitrogen is produced by bacterial decomposition of dead organic matter (e.g. animal excreta, dead plants or animals). In a sterile soil the nitrogen in this organic material would not become available to green plants. Under certain circumstances, as was shown by Russell, in 1909, even in a soil with a relatively considerable microbial population, there may be a failure to convert organic nitrogen to available inorganic forms, so that one may have a soil rich in nitrogen but infertile as measured by the growth of crop plants. This type of infertility, commonly spoken of as 'soil-sickness,' is not infrequently met with in soils receiving very heavy dosages of organic matter, such as in sewage farms and glasshouse beds. It can be overcome by partial sterilisation of the soil, that is by application of disinfectants such as formaldehyde, cresylic acid or toluene or by a mild heat treatment. This treatment causes an initial reduction in bacterial numbers followed by a very marked increase and an accumulation of inorganic nitrogen from increased decomposition of organic material. Partial sterilisation has a similar effect, though less marked, on normal soils not suffering from soil-sickness.

By various experiments Russell demonstrated conclusively that the soil-sickness was due to living organisms less resistant to the sterilisation treatments than the bacteria responsible for the breakdown of organic nitrogen.

On this basis he postulated, but was not able to prove rigidly, that the antagonistic organisms were the soil protozoa. These organisms are actively predatory and ingest large numbers of bacteria. Russell suggested that the soil-sickness was associated with a great increase in numbers of protozoa which, by their predatory activity, reduced bacterial numbers and this slowed down the breakdown of organic matter in the soil.

Partial sterilisation might then be supposed to kill the protozoa to a greater extent than the bacteria, and Russell showed that they were less resistant than the bacteria, thus restoring a microbiological balance conducive to rapid breakdown of organic matter. It is generally accepted that soil-sickness is due to a lack of microbiological balance of this type, but the major rôle attributed to the soil protozoa by Russell has not been so generally accepted.

At that time (1909), when no mechanism was known whereby one group of soil microorganisms might effect the numbers of another group, other than by active predatory attack or by more efficient utilisation of available foodstuffs, it was perhaps inevitable that the protozoa, whose predatory habits were known, should be given most attention in attempts to explain the observed phenomena of soil-sickness and partial sterilisation. With our newer knowledge of the production of antibiotic substances by soil microorganisms other explanations can be suggested. The partial sterilisation procedures first used by Russell also reduce the numbers of soil fungi and actinomycetes much more than those of the bacteria mainly responsible for the breakdown of organic matter. Many of these fungi and actinomycetes produce antibiotic substances highly toxic to bacteria, and a reduction in their numbers might well be expected by reduction in the amount of the antibacterial substances produced, to lead to the increase in bacterial activity noticed after partial sterilisation. This is a plausible theory, but still requires experimental proof.

The influence of the production of antibiotic substances on soil fertility can also probably be seen in other ways. Subsoils are much more inert than top soils. The number of microorganisms present is less and plant materials which would decay rapidly in top soil are broken down much more slowly in subsoil. This is not due to lack of nutrients in the subsoil, but appears to be due to the presence of inhibitory substances. This can be demonstrated quite easily. If one has a quantity of sand on the one hand, entirely free from nutrients, and a quantity of subsoil on the other hand, mixes with each a little top soil, and places a little straw in each, the straw is much more quickly decomposed in the inoculated sand. Further, alcoholic extracts of subsoil added to a top soil very markedly reduce microbiological activity in the latter. To explain these observations it has been suggested that inhibitory (antibiotic) substances produced by microorganisms in the upper layer of soil accumulate in the lower layers as a result of leaching.

Another, in many ways more striking, case of microbiological unbalance affecting soil fertility has recently come to light, which also may be associated with the production of antibiotic substances. This case is concerned with a growth failure of pine trees in an afforestation area at Wareham Heath, Dorset. In certain areas pine seedlings make little growth and eventually die out. Coniferous trees, indeed most if not all trees, are very closely dependent on certain elements of the soil microflora. Associated with the roots of these trees are certain soil fungi, the tree and the fungus forming by mutual co-operation distinctive organs, on the tree roots, known as mycorrhiza or 'fungus-roots.' The function of these is not known but their necessity for optimal development of many trees has been demonstrated. The soil at Wareham Heath contains something antagonistic to the mycorrhizal fungi, which fail to form the necessary association with the coniferous trees, with the result that the latter do not develop properly. Rayner and Neilson-Jones, by whom these observations have been made, showed that this antagonism was of biological origin and suggested that sulphate-reducing bacteria were present in excess and were producing sulphuretted hydrogen (which could in such a case be regarded as a very simple antibiotic substance) which was toxic to the mycorrhizal fungi. Other workers have suggested that the antagonism may be due to the production of gliotoxin and other unidentified antibiotic substances by a number of species of the mould *Penicillium*, which are unusually abundant in this soil.

All these examples indicate how microbiological balance may affect soil fertility. There is reason to suppose that one of the methods by which this balance is maintained is the secretion of antibiotic substances. What has not yet been properly explained is why under certain circumstances such marked states of unbalance arise.

The production of antibiotics has also a close relation to problems of public health. One can imagine the situation that would arise if human pathogen bacteria falling into the soil and water-basins were to multiply there, or even survive for long periods. Some do not survive because they have specialised temperature or nutrient requirements. Some will survive for long periods in sterile soil or water, whereas they disappear rapidly in normal soils or waters. There is strong presumptive evidence that their disappearance is due to the activities of antagonistic microorganisms, some of which, at least, act by the production of antibiotic substances.

The study of antibiotic substances has so far been mainly directed to finding antibacterial substances of medical interest. The balance of microorganisms in the soil is regulated at least in part by the excretion of antibiotic substances by some of them, and the effects of these probably extend to types of organism, such as protozoa and nematodes, that have not yet been studied in this connection. It is reasonable to suppose, therefore, that a broadening of the researches on antibiotics would not only provide us with new antibacterials, but also with new fungicides, anthelminthics and anti-protozoals. Apart from these more immediately human benefits, a study of the effects of different antibiotics on the different types of organism occurring in the soil, in the conditions of their natural habitat, will give a much greater understanding of the factors responsible for the balance of microorganisms in soil, which may in turn lead to a much more fundamental knowledge of the relation between soil microorganisms and soil fertility.

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WEEDS OF CORNFIELDS

By Winifred E. Brenchley and H. C. Long

Photogravure illustrations between pp. 80 and 81.

WHEN townsfolk admire heavy crops of corn—be these wheat, oats or barley—how often do they consider what has been done to bring about success? What can most of them know of soil formations and their needs, of cultivation, liming and manuring, choice of seed matched to soil and climate, resistance to disease or to wind and storm—or to competition with weeds for light and air and standing-space and food?

It was once said by a Bishop of Carlisle that agriculture is a controversy with weeds—a very true observation. Weeds are also held to be plants out of place, plants growing among crops sown or planted by man and hence where they are not wanted.

Weeds of cornfields are numerous both as to species and as to quantity. A cereal crop is commonly preceded by a 'cleaning' crop like roots, in which weed seedlings are destroyed by repeated hoeings; or by a hayed or grazed clover or grass-and-clover crop, the residue of which is ploughed under for the help of the grain crop.

This notwithstanding, all soils in practice contain vast numbers of weed seeds, often at the rate of many millions per acre. Cereals sown in autumn—and most of our wheat is sown then—occupy the land for a long time, say eight to ten months, and this affords an excellent opportunity for weed seeds to germinate, mature and scatter more seed upon the ground before and when the cereal is harvested.

Not only do many weeds produce enormous numbers of seeds, but these seeds are in very many instances capable of great resistance to destructive influences like cold and heat and wet, when buried in the soil. They may, therefore, lie dormant for many years and then germinate, and attain maturity, when conditions are favourable.

To illustrate the rate of seed production of some important arable-land weeds it may be observed that single plants of the following may produce the number of seeds mentioned; corn cockle, 400; charlock, 4,000; field bindweed, 600; cleavers, 1,100; corn marigold, 13,500; scentless mayweed, 310,000; annual sow thistle, 3,000 to 19,000; groundsel, 300 to 20,000; poppies, 50,000.

There is a great accumulation of data as to the vast quantities of seeds produced by weeds, the almost incredible millions that have been found in an acre of arable land, and the long years over which viability may persist. On some of the permanent wheat plots on Broadbalk field at Rothamsted living weed seeds have been proved to be present at the rate of 300,000,000 per acre, and seedlings of various weeds were still being obtained from seeds left in soil samples after ten years of intensive cultivation.

It is also to be borne in mind that the weeds of cornfields may be low-growing and humble annuals like corn pansy, lady's mantle, scarlet pimpernel; others like charlock, runch and corn marigold, may grow tall and large; while yet others like creeping thistle, perennial sow thistle, field bindweed, are extremely persistent perennials that have creeping rootstocks, and may attain a most remarkable prolificacy and abundance.

On comparatively weed-free or 'clean' soils the injury done to cereal crops by weeds may be almost negligible, but when land is fouled it may be fatal to sow corn upon it until it has been put through a thorough course of cleaning and root crops. In an instance known to one of us (H. C. L.) a very badly weed-infested field was ploughed seven times, apart from other cultivations, before the sowing of any crop! Happily it was rent free for the first year.

The actual injury caused by the presence of weeds is to rob the cereal of air and light (and warmth), and deprive it of water and plant food that might, from the human point of view, better have gone to increase the corn crop. If the pressure of weeds on the corn crop is very severe the cereal yield may be heavily reduced. As an example, the difference between a clean barley crop and a weed-infested one was shown to reach a loss of 46 per cent in money value.

Another cause of loss due to weed infestation is the extra cost of cleaning thrashed grain from the included weed seeds. This may be especially bad when wheat is infested by the wild onion, the bulbils of which are about the size of wheat grains, and unless removed impart an onion flavour to the grain products. The presence of either darnel or corn cockle renders the cereal unsafe until it is removed, both these weeds having toxic properties.

In some instances weeds may make corn harvest much more troublesome, as when field bindweed and black bindweed infest the crop and drag it down; or when the creeping thistle, present in quantity, causes annoyance to both men and horses at harvest, as well as at thrashing time, and reduces the value of the straw.

Finally, weeds may act as hosts for certain insects and fungi injurious to cereal and/or other crops, while it is worthy of mention that red bartsia, and also the greater yellow rattle, may be parasitic on the roots of cereals and on occasions do considerable damage.

Weeds of cornfields naturally differ as widely as plants that grow in other situations, and they may be annual, biennial or perennial, belong to many Natural Orders, and vary considerably in accordance with the type of soil, while some are destroyed with much greater difficulty than others.

It may be said, for example, that poppies are most prolific on the lighter fertile soils, and seem to grow best when kept damp in early spring. Yellow charlock is an annual that is, in most areas, perhaps the most troublesome of all cornfield weeds—but it has hitherto been more easily destroyed by spraying than runch or white charlock.

It is, of course, widely recognised that there is an association between weeds and soils, but the line of demarcation is not in the least definite. A certain weed species may be much more closely associated with one soil than another, but it may nevertheless be possible for it to be a serious pest on its 'less usual' soils. For example, the wild carrot, dandelion, scarlet pimpernel and tall buttercup may be described as having a definite preference for chalk soils—but they certainly occur in plenty on most soils.

Of weeds of cornfields the field pansy, bladder campion, white campion, corn gromwell, fumitory, red bartsia, scarlet pimpernel and lady's mantle are more partial to chalky soils than others. Spurrey, corn marigold, marsh cudweed, annual knawel and annual nettle are characteristic of sandy, light soils. The perennial sow thistle, charlock, field madder, shepherd's needle, runch or wild radish, poppies, field forget-me-not, corn cockle, cleavers, field bindweed, creeping thistle, shepherd's purse, black bent, will grow quite plentifully on most soils, especially loams in good condition. The wild oat and slender foxtail are partial to heavy land.

Nevertheless, various weeds from these rough groups may occur together in the same crop.

Coming to the question of eradicating weeds of cornfields, it should be said that in centuries gone by hand pulling of weeds was the common lot of the farm worker. Indeed, in his younger days, one of the authors of this article did quite a lot of hand pulling where charlock sometimes got the better of the farming! This was before spraying was introduced.

The horse-hoeing husbandry of Tull went far to keep weeds within bounds, and then for generations wheat was regularly hand-hoed, drill husbandry making this much more easy as compared with broadcasting. The four-course rotation—roots, barley, clover, wheat—and its variations were designed to keep the land clean under different systems of farming, and provide for the needs of individual crops.

During profitable periods, farmers as a body would carry out necessary tillages and hand-work to keep down weeds to a minimum. Always, however, recurring times of slump and loss led to incapacity to carry on high farming, and weeds increased.

In recent years the coming of sugar-beet, with the cleaning necessary for its successful cultivation, has greatly helped weed suppression on very large areas.

In general, annuals are for the most part much more easily combated than perennials.

Such perennials as docks, creeping thistle, perennial sow thistle and wild onion are combated in the main by mechanical means, in the rotation, but on occasion in cereals they must still (except wild onion) be hand pulled if the crop is not to be severely reduced. Spraying may, however, have a sufficiently injurious effect on some perennials, especially when they are in flower, to prevent them from ripening seed.

In many instances a well-grown cleaning crop, or even a bare fallow or special method, may be requisite to reduce perennials before the cereals are grown, or extra expense will be necessary afterwards. Many workers can readily recall the most unpleasant experience of trying to load sheaves of a corn crop very completely infested with ripe creeping thistle! Such events are bound to occur on occasion, even with the best farming.

It is a much simpler method to deal with the weeds in spring-sown cereals than in cereals sown in autumn.

In general, weather conditions prevent much being done after winter corn is well advanced, until spring days arrive. Many sprouting weed seeds may be killed by tillages before spring corn is sown, during those March days when a peck of dust is worth a king's ransom. Then, too, spraying of spring corn to kill weeds is simpler than with winter corn, which is often well advanced by mid-March.

During the past six war years the necessity was laid upon us to grow corn twice and even three times in successive years upon the same land, so immensely increasing the chances of weed infestation, no 'cleaning' crop intervening. After harvest, autumn surface cultivation had to be used to the full to encourage weeds to grow, for destruction by further cultivations and by ploughing the weeds down before the next grain could be sown.

Nevertheless, so heavily do some cornfields become weed-infested that other steps may be necessary to destroy the weeds. These steps may include surface harrowing in spring, but best of all is spraying with a substance toxic to weeds but not to the cereal.

Mechanical methods of weed eradication are directed to the complete removal of the plants from the soil, or towards such severe mutilation that further growth is either impossible or so weakened that the competition with the crop is reduced to a minimum.

Spraying methods, on the other hand, deal with the weeds *in situ,* and are aimed either at interfering with the physiology of the plant in such a way as to cause death, or at destroying the tissues by corrosive action, again hindering the normal processes of growth. Some sprays work by direct action on the leaves, some may also be translocated down through the stems, while others may pass to the roots by way of the soil, where they are absorbed and help to kill the plant in that way.

Modern research is constantly seeking for new materials to use as sprays, in order to increase the range of susceptible weeds and to render the results of spraying more reliable and less dependent on the vagaries of the weather, especially in such a variable climate as that of Britain. Many chemical substances have been investigated during the last few years in order to discover materials that will control a greater range of weeds, or that may be less likely to damage the crops. Only time and experience will tell if they can establish themselves in the same position as sulphuric acid and other well-known sprays.

The fundamental reason why a poisonous spray can be used in a growing crop lies in the difference in habit between crop and weed. To act effectively a weed-killer must be able to retain its position on the plant long enough to dry out and start its deleterious action on the tissues. Cereals are thus relatively immune from harm, as the spray fluid runs down the blade before it can establish itself. Plants with waxy leaves also usually escape injury, for the fluid collects into balls and rolls off, even from broad-leaved plants. This occurs whether the plants are crops or weeds, as Nature does not recognise this man-made distinction.

On the other hand, the spray is collected on broad-leaved plants, whether they be crops like clover or weeds like charlock. In spite of all research it has not been possible to devise any spray that can make this distinction and kill charlock while leaving clover undamaged—and indeed it is difficult to imagine that this will ever be done successfully. What is being done, however, is to take advantage of the fact that some species are more easily damaged than others by a particular chemical, and to choose the spray according to local conditions.

Another important factor is that plants are more susceptible to damage at some periods of their lives than at others. Young seedlings are usually very tender and can often be eliminated if attacked at this stage, but may become more resistant later, the leaves developing a thick cuticle or a waxy coating that acts as a protective agency.

Plants may also become more susceptible when the relatively unprotected flowering shoots emerge, and spraying at this time may be useful in preventing seed production, though it will be too late to prevent damage to the crop from competition for food, light and water used by the weeds in their development.

Another biological factor that affects the efficiency of sprays is the degree to which the growing point is protected. If this point is tucked away within some protective envelope, as within the sheathing leaves of grasses and cereals, it does not matter much if the outer leaves are damaged, as new growth will soon replace them. This also occurs with many deep-rooted perennial weeds, which can send up fresh shoots from buds hidden away below ground, even when the shoots above ground have been entirely destroyed. When the buds are exposed in the angles betwen the stems and leaves, and at the apices of the shoots, they are killed as well as the leaves, and regeneration is not possible.

Generally speaking, therefore, the control of weeds by spraying has chiefly been considered in relation to cereal crops, which have the ideal habit that enables them to escape unscathed from the action of poisonous fluids or dusts, or else to be relatively little harmed so that they soon throw off any ill-effects and make their normal growth. As one of the principal weeds among cereals is charlock, it is often thought that this is the only weed that can be controlled effectively by this method, but modern research shows that this is by no means correct.

Spraying for weed eradication or control is by no means confined to corn crops, but can be used where it is desired to destroy all vegetation, as on paths, tennis courts, and railway tracks. In such instances it is necessary to use substances that will kill the plants regardless of their biological habit, by acting through the roots, or by adhering to the surface in sufficient quantity to cause the requisite damage. Sometimes this can be done by using the ordinary weed sprays in greater concentration. Various oils, tar-oil distillates, sodium chlorate, sulphuric acid and caustic soda can all be used as *non-selective* weed-killers for this purpose.

In cornfields, however, only the *selective* weed-killers are of any value, apart from the question of destroying the stumps of trees and shrubs when hedges between fields are cut down. It may be advisable to give a word of warning here at the risk of repeating what has already been said. The term 'selective' weed-killer has been over-emphasised in recent years, leading to some misapprehension and possible disappointment.

Selectivity is not between the weeds and crops, but between plants of different habit or with other morphological characteristics that render the plants susceptible or resistant to the spray fluid or dust. The number of substances that have been used as selective weed-killers is considerable, and modern research is reaching out after a still wider range, seeking to employ certain physiological reactions of the plants to the spray fluids instead of depending on mere physical damage. For instance, the production of root initials may be greatly increased and hastened, sometimes to such an extent that they are unable to emerge properly and fail to develop, so that the roots become distorted and unable to function properly.

Many of the common sprays are poisons that kill the weeds but do not exercise any directly beneficial action on the crops, whereas others are fertilisers that first destroy the weeds and then pass into the soil to play their part in improving crop growth. The choice of spray depends upon various factors and is governed to a great extent by local conditions. Where water supply is a limiting factor, dusting may be more feasible than wet spraying. If land is both weedy and poor the extra expense of spraying with fertilisers may be fully justified, while in other instances the use of a straight poison may be more economical. It is impossible to lay down any hard and fast rule as to the best course of action, as every case must be considered on its own merits and dealt with accordingly.

The discovery of the possibility of controlling weeds by the use of chemicals followed as a corollary to the standard method of spraying vines with Bordeaux mixture to prevent disease. About 1897 a French vine grower noticed that charlock plants were blackened wherever Bordeaux mixture happened to fall on them. This was followed up by much experimental work in this country and elsewhere, the active agent being established as the copper sulphate in the spray.

At first farmers were naturally suspicious, in the true tradition, but gradually the new method of weed control proved its value and in many places charlock spraying became accepted as part of the farm routine. Even now, however, spraying is more usually done on the larger farms, as the seasonal nature of the work and the expense of effective equipment renders it a more difficult proposition on smaller areas.

Co-operative ownership of spraying tackle does not altogether meet the needs, as all the partners are likely to need the machine at the same time, when the weeds are at the appropriate stage and weather conditions are favourable. This difficulty may be met to some degree by the development of spraying materials that will remain efficient even if rain follows soon after their application, thus extending the period during which the work can be done.

The earlier experimental work was carried on by agricultural colleges and county councils all over the country, and showed that the strength of the spray and the quantity necessary per acre vary according to circumstances, climatic conditions having a direct bearing on the matter. In the drier parts of the country, as in East Anglia, smaller quantities of a weaker solution are as effective as larger amounts of a stronger solution in the wetter areas in the West Country. For instance, given suitable weather, 50 gallons per acre of a 3 per cent solution of copper sulphate may suffice in drier districts, whereas a 4 or 5 per cent solution is necessary for success in moister places, as in North Wales. This does not apply only to copper sulphate, but has to be considered with all types of sprays.

Copper sulphate, iron sulphate and sulphuric acid form a group of corrosive substances much used for spraying. All are effective against charlock, and attack certain other weeds as well. Wild radish, though closely allied to charlock, is more difficult to kill on account of its hairy leaves, and may need a second treatment at a later date to destroy it completely. Poppies are susceptible provided they have been crushed or trodden down before spraying, but spurrey, so prevalent on light acid land, does not respond so well and is apt to develop a secondary growth from the roots, producing flowers and ripening seed before harvest.

Perennial weeds are less effectively controlled by these contact sprays, for though the leaves may be destroyed fresh growth soon springs up from the crown or from subterranean buds, and the weeds continue to flourish. Iron sulphate is not very popular in this country, as it has the disadvantage of deteriorating on keeping if the crystals are fine, while large crystals take longer to dissolve. It costs less than copper sulphate, but 10–20 per cent solutions are needed instead of 3–5 per cent, this equalising the actual cost of the two materials.

In modern practice both of these sulphates have largely been superseded by sulphuric acid. Our knowledge of this spray owes much to Korsmo and his colleagues, who carried out exhaustive controlled experiments over wide areas of Norway, comparing the effect of sulphuric acid spraying with that obtained by other methods. This fine example of teamwork stood out alone for many years, and has only recently been paralleled by that of G. E. Blackman and his colleagues in this country, working on a variety of sprays.

Sulphuric acid acts very quickly, and rain following soon after spraying is not such a disadvantage as with the sulphates, since the weeds are killed so rapidly. With all three of these sprays the outer leaves of the cereal crop are apt to be more or less touched and browned, as they spread out sideways, but the new leaves quickly develop from the protected growing points and very soon the initial damage disappears and the plant shows no further ill-effects.

One serious disadvantage is the corrosive nature of all these materials, and special precautions have to be taken, particularly with the acid. It is essential that the amount of acid needed be poured into a much larger quota of water, as water poured into acid generates a dangerous amount of heat and may cause severe personal injury. Splashing of personnel and clothing must be carefully avoided, and the spraying equipment must be very thoroughly washed out with clean water immediately after use, as the acid attacks all metal parts very rapidly. The acid must be mixed in wooden barrels and stirred with a wooden stick before being poured into the spraying machine. As acid spraying slightly reduces the lime content of the soil, it is advisable to redress the balance by the application of 1½–2 cwts. of lime per acre after each treatment.

Sulphuric acid is generally used in the commercial form of brown oil of vitriol, commonly known as B.O.V., which contains about 75 per cent of pure sulphuric acid. The concentrations needed vary with the dominant weeds to be destroyed, ranging from 7 gallons B.O.V. per 100 gallons of spray solution for pennycress and cleavers, to 15 gallons for corn buttercup and shepherd's needle. As a general average 10–13 gallons are used, as this suffices for most of the prevalent weeds like charlock, wild radish, chickweed and spurrey.

For some species, as fat-hen, mayweed, knotgrass and corn marigold, the acid spray is not effective without the addition of a small quantity of a wetter and spreader to help the spray to adhere to the leaves, sulphonated oils being more suitable than soft soap for this purpose. As cereals depend for their immunity to injury on the spray being able to run off before it has time to damage the leaves, the use of too much wetter and spreader may cause harm to the crop as well as to the weeds with broad leaves, and only 1 lb. of dry material or 1 pint of the liquid per 100 gallons of spray should be used.

Copper chloride is another good weed-killer, and for some weeds is a satisfactory alternative to sulphuric acid. It readily absorbs water from the air and is usually marketed as a strong solution in carboys. It acts more slowly than the acid and is therefore more dependent on good weather conditions, and though it does not damage clothing or injure the skin it is more corrosive to metals. The equivalent of from 4–9 lb. of dry copper chloride is needed for 100 gallons per acre, but some weeds, as knotgrass, are resistant to it, and information about many other common weeds is not yet available.

A wetting agent should never be used with copper chloride owing to the increased risk of damage to the crop. Copper chloride is specially effective against charlock, pennygrass, black bindweed and treacle mustard, but other important weeds are resistant to its action, including poppy, fat-hen, corn buttercup, shepherd's needle, knotgrass, mayweeds, and fumitory.

Artificial fertilisers may also be used as sprays and dusts, as they either corrode the leaves or kill them by encouraging rapid plasmolysis or withdrawal of essential water from the tissues. They have never come into general use for this purpose, though there are circumstances when they prove their value, particularly on land that will profit by the particular fertiliser after it has done its work as a weed-killer. Ammonium sulphate at 1 or 2 cwts. per acre dissolved in 60 gallons of water has been successfully used among cereals, while increasing the yield as much as 7¾ bushels per acre with oats, and from 2–4 bushels with wheat and barley. Corn buttercup, hoary pepperwort and spotted medick can be controlled in this way, but charlock does not respond so well unless the plants are very young. It is essential to spray early in order to allow time for the crop to profit by the manurial value of the solution, as otherwise the method is uneconomic.

On land that responds to potash, dusting with kainit is a good means of controlling charlock, the extra profit depending largely upon the time the work is done, as late dusting means a smaller increase in crop owing to the effect of competition before the weeds are checked.

Calcium cyanamide is another nitrogenous fertiliser that can be used as a dust, but during the war the material was not obtainable and so no recent work has been done to compare it with the newer weed-killers.

The earlier sprays were mostly inorganic substances or fertilisers, but during recent years various organic compounds have been tested for their possible herbicidal value. Among the most promising of these is di-nitro-ortho-cresol (often called D.N.O.C.) and its derivatives, which are also much used as insecticides. D.N.O.C. is a yellow dye produced from the by-products of coal distillation, and though it is not very soluble its compounds dissolve more easily and are thus more generally useful as weed-killers. When these substances are dry they are inflammable and are therefore marketed in the form of pastes with a specified quantity of water to enable solutions of known strength to be made up.

The sodium salt, under the name Sinox, was first used in France in 1933 and introduced into the United States four years later, where it proved most efficient, being used over large acreages. Sinox works best when it is combined with an activator such as ammonium sulphate or sodium bisulphate, which hastens the action and makes it more effective. The bisulphate is preferable when there is any risk that extra nitrogen may encourage cereals to lodge or fall over from the lower joints of the stems before the ears are ripe. Treatment with 1 gallon of Sinox in 100 gallons water per acre is effective against charlock, though heavier doses are needed for more resistant weeds such as wild radish, fat-hen, chickweed and knotgrass. The younger the weed, the less Sinox is needed to kill it, and it is therefore most important to attack only the resistant weeds in the early seedling stages, as heavy doses of Sinox cause serious damage to cereals.

Temperature has much to do with the effectiveness of Sinox, as if it is too low at the time of application or if the weather has previously been too cold or extremely dry the weeds are not killed, but this difficulty does not arise when an activator is used. The lethal action is slow, even under favourable conditions, but the spray holds fast and is not easily washed off even if rain follows soon after application. There is no risk of the soil being damaged by the spray, as Sinox is soon decomposed by microorganisms without leaving any toxic residues.

After the outbreak of war it became impossible to obtain Sinox in this country, but similar compounds have been developed and tested. D.N.O.C. paste and the copper and ammonium salts are used without activators, but the sodium salt is more effective with the addition of ammonium sulphate at the rate of 10–20 lb. per acre. Cereals soon recover from any initial damage due to spraying, provided that the recommended dosage is used, but larger quantities may do considerable harm. Claims are made that peas and beans are immune from harm, but there is no adequate proof of this.

Care is also needed in the selection of the particular compound, as one may cause more damage to the crops than another. Among cereals these weed-killers can be used successfully at various stages in the growth of the crop, but as a general rule it is best to spray while the weeds are in the seedling stage, when they are most susceptible.

More research is needed to eliminate or reduce certain disadvantages of all these substances. The necessity for marketing them as pastes that are not easy to mix makes it difficult to ensure that successive batches of the spray fluid are of the same composition, and as the material tends to settle out it is necessary to keep the spray agitated. If there is no mechanical agitator on the spraying machine the insoluble D.N.O.C. should not be used, and it should be replaced by the more soluble ammonium or sodium salts.

Also, as all these substances are dyes they stain yellow everything with which they come in contact, so that protective clothing is necessary, especially as the stain is very difficult to remove from the skin, hair and clothing. Apart from this, however, D.N.O.C. and its derivatives are perfectly harmless to human beings, while they are very toxic to many plants. Further experiments to improve the preparation of the materials are very desirable in order to render them more easy of application.

Other materials that are being tested for their possible use as weed-killers are some of the hormones or growth substances. One of these, Methoxone, also called C.L.C.

or Corn Land Cleaner, shows special promise, and has been distributed by Imperial Chemical Industries during the last season to the war agricultural committees and the research stations for wide-spread tests. The results are obviously satisfactory, and it was announced that the material would be put on the market under the name of Agroxone.

It is not possible to forecast how this new weed-killer will compare with the older types until several years' results are available, as variation in seasonal conditions may affect its working. It acts through either the roots or the leaves, and is independent of weather conditions. It can be used in liquid or dust form, and as very small quantities are required the dust is sent out diluted to 1 per cent so that it can be applied as a top dressing by means of fertiliser drills.

Agroxone behaves quite differently from any other weed-killer, and for some time little result is to be seen. Then the affected plants begin to become curled or otherwise deformed, gradually dying as the hormone makes its way through the plant and acts on the tissues. It must not be used on cereals undersown with clover, even if the seeds are not sown till after the weeds have been sprayed, as it is not known how long it is necessary to wait before the danger to young seedlings has passed.

The extensive experimental work in 1945 showed that various weeds in cereals and grass land were affected by Agroxone in the following order of susceptibility:

Complete control	*Seriously affected*	*Affected*	*Unaffected*
Yellow charlock	Corn marigold	Bindweed	Bladder campion
White charlock (Wild radish)	Fat-hen	Spurrey	Coltsfoot
	Speedwell	Thistles	Cleavers
Pennycress	Chickweed	Mayweed	
Corn buttercup	Poppy	Polygonum spp.	
	Sow thistle	Dock	

Special care will need to be taken that such potent materials are not applied, by accident or design, to susceptible plants that are not weeds. For instance, the deadly effect upon yellow charlock indicates the danger of allowing these new weed-killers to drift over any cultivated crops of the cabbage family.

Most of the experimental work so far has been in connection with weeds in cereal crops. The work is being extended to grass land, and it is already clear that some of the worst weeds, as creeping buttercup, are controllable by this means, and there is every reason to believe that the method will be effective against dandelion, daisy and plantain, which cause so much trouble on lawns and sports grounds.

A question often raised is whether spraying is of economic value in increasing the financial returns on the crops concerned. That it is so was clearly demonstrated about twenty years ago by a large number of controlled experiments carried out in various places, in which detailed costings and returns were kept. Spraying is not justified unless the weed population is sufficiently large to come into direct competition with the crops, as otherwise the removal of the weeds would make very little difference to the crop growth and yield and cost of spraying might not be recovered.

Where weeds are plentiful, spraying carried out at the right time and with favourable weather conditions was shown to be very profitable. The costs include the labour of men and horses, the price of the spray materials, and the value of depreciation and repairs—a very considerable item. The total costs, at the prices ruling at that time, varied from 5*s.* 10*d.* per acre with iron sulphate to £1 11*s.* 2*d.* with a heavy treatment with ammonium sulphate, and these costs could be covered with a handsome surplus by the value of the increased crop resulting from the spraying.

Similar treatments repeated at different places or in different years gave varying results, depending on the degree to which the conditions favoured success. The range of increased value obtained in these experiments, after all costs have been met, is shown in the following table, relating to wet and dry spraying:

Crops	*Spray material*	*Increased value per acre due to spraying after all costs have been met.*
Wet spraying		
Oats	Copper sulphate	£1 2*s*. 7*d*. to £8 8*s*. 9*d*.
Oats	Iron sulphate	£2 10*s*. 9*d*. to £5 0*s*. 2*d*.
Oats	Sodium nitrate	£1 14*s*. 4*d*. to £5 13*s*. 3*d*.
Barley	Copper sulphate	£1 11*s*. 4*d*.
Wheat	No figures available	
Dry spraying		
	Kainit, applied early	£3 10*s*. 5*d*.
	Kainit, applied late	£1 16*s*. 8*d*.
	Calcium cyanamide	£4 7*s*. 6*d*.

The above figures were all based on results under ordinary field conditions. Some are very considerable, but they show that it is possible to reach a high level of extra profit, and even if the values were very much lower it would still be a paying proposition to spray where the weed competition threatened the development of a full crop. Similar figures have probably not been worked out for the newer sprays, and the balance of costs is now very different, but with the prices of farm products at their present level a relatively small increase in yield would amply repay the cost and trouble of spraying.

Since the main object of spraying is to remove the competition of weeds with the crop it is not essential that all the weeds should be eradicated, but that they should be controlled. Destruction of the majority of the weeds at an early stage of growth enables the crop to grow away strongly and itself come into competition with the remaining weeds, which are then unable to develop sufficiently to do much damage.

Comparing the results that have been obtained with the various materials tested, it remains evident that sulphuric acid, with all its disadvantages, has up to now given the greatest measure of control. A very heavy kill can be obtained with many of the worst weeds, and some of the more resistant ones can be controlled if a wetter and spreader is added to the spray. D.N.O.C. and its compounds are also very generally useful, but with copper chloride and Agroxone a larger number of species are resistant and not killed by treatment.

The choice of spray must be determined by the weeds that most need control, and to some extent by local weather conditions and the labour and equipment available. As time goes on it is to be expected that spraying will become more of a routine measure on the farm than it is now, and it may be hoped that further experiments will render the technique more easily carried out by farmers on all types of land in different parts of the country.

BAT 'RADAR'

By Richard H. Knight

No one can fail to have been impressed by the facility with which bats avoid obstacles while flying even at high speeds. Whether in daytime or in complete darkness their power of navigation is unsurpassed. Not only can they steer clear of trees and houses, but laboratory tests have shown them to be capable of avoiding wires only 1 mm. in diameter in complete darkness. It is not surprising that numerous attempted explanations bordering on the magical should have cropped up from time to time. Probably the only feasible hypothesis—put forward in 1920—was contained in Professor Hartridge's suggestion that they might well make use of *supersonic waves.*

It is well known that the sounds which stimulate our ears reach us as periodic vibrations or waves in the intervening air. These waves arise from periodic oscillations about their mean position of the molecules in the air. No molecule makes a net movement in the direction of the sound-waves, but each communicates its oscillatory motion to the next molecule. The result of these molecular vibrations is that at any fixed point the air is alternately compressed and rarefied. A complete wave extends from one point of maximum compression to the next. The distance between these points is the *wavelength* of the sound, and the longer this is, the lower will be the *frequency,* i.e. the number of waves passing a given point in a second. Variations in *pitch* are the sensory consequence of variations in frequency. There is, of course, a wide range of such air vibrations and only a comparatively narrow band of them have any effect on the human ear (30–20,000 cycles/second). These are called 'sound waves,' while to those whose frequency is above the human audible limit the name 'supersonic waves' has been given.

As we shall see, much evidence has recently been accumulated which supports the view that bats can both emit and hear supersonic waves. These waves are supposed to be reflected from nearby objects, and from the direction of the reflected waves the bat could learn something of their whereabouts. The mechanism has added interest in these days on account of its similarity with the technique of radar. In radar the place of supersonic waves is taken by high-frequency radio waves, which are of the same nature as light—though invisible—and which do not depend on a material medium like the air for their transmission.

Before the hypothesis can be accepted as the correct one several kinds of information are required:

(*a*) What properties must the vibrations have for them to be of any use to the bat?
(*b*) Is the bat able to produce such vibrations?
(*c*) Is the bat's ear sensitive to them?
(*d*) If the answer to the last two questions is in the affirmative, we must find out whether the animal's behaviour is modified if we prevent either the emission or the reception of the vibrations or both.

Let us proceed to try to answer these questions.

It is a well-known property of all kinds of wave motion that the longer waves (lower frequency) are less readily deflected from their course than the shorter ones (higher frequency). Two illustrations are familiar to all. Larger waves on the seashore pass piers and groynes with little change in either their form or their direction, whereas ripples are reflected and scattered in all directions. The red lights which predominate at sunset have their origin in a similar effect. Light consists of electromagnetic vibrations whose frequency determines colour in a way analogous to that in which the frequency of sound-waves determines the pitch of the sound. The sensation of red is produced by waves of relatively lower frequency than that of blue. At sunset the light from the sun has to traverse a considerable thickness of air containing dust and smoke and water vapour. These particles scatter the short-wave blue light, leaving the light we receive with a greater proportion of the longer wavelengths.

To return to our air vibrations, it is found that for enough reflection from thin wires, waves of audible frequency are quite useless. Calculation shows that to obtain a reflected beam from such a small object with sufficient intensity the vibrations must have a frequency of the order of 50,000 cycles/second. This is nearly two octaves above the limit of the sound-waves.

Do bats emit these vibrations? Recent work, notably by Galambos and Griffin in America and their co-workers, shows that in addition to the familiar audible squeaks bats do in fact emit supersonic vibrations. The experiments are carried out by placing microphones near to flying bats. The function of the microphone is to transform the purely mechanical vibrations of the air into periodic variations in an electric current or potential difference of the same frequency. These electrical vibrations can then be examined by means independent of a hearing organ, for example visually on the screen of a cathode-ray oscillograph. Such experiments leave little doubt that bats emit supersonic waves within the frequency range 30,000–70,000 cycles/second. It is noteworthy that this range is of the same order of magnitude as the frequency we have seen to be desirable. Moreover, the vibrations are not emitted continuously but in short pulses, the time beween successive pulses varying according to the proximity of an obstacle. Thus a stationary bat gives out only a few such pulses each second, while on beginning to fly the rate becomes 20 or 30 per second—increasing to 50 or 60 per second as an obstacle is approached. The advantages of this are clear. As an obstacle gets nearer it is desirable to 'sound' more frequently since there is less time to make avoiding movements. Further, the time for the vibrations to reach the obstacle and return is also shorter, so that consecutive pulses are less likely to become confused. Thus when an obstacle is close rapid pulses can be used for frequent sounding without overlapping of signals. An analogous procedure is adopted in radar.

The answer to our third question is equally clear. Although the bat's cochlea (the sound-sensitive organ of the ear) is similar to that of other mammals, it is modified to allow perception of these very high frequencies. When sounds fall on the ear of a mammal, or in fact of any animal with a similar sensory mechanism, it is possible to detect electrical changes in the auditory nerve. A pair of electrodes is inserted, one in the auditory nerve and the other in some other convenient part of the body of the anæsthetised bat, and wires from these are led to amplifiers and hence to some electrical recording device. Over the range of frequencies to which the ear is sensitive vibrations from another animal or from a purely mechanical source are accompanied by characteristic changes in electrical potential difference between the electrodes. Galambos has used this technique and finds that the bat's ear is sensitive to frequencies at least as high as 98,000 cycles/second.

Finally, how are these facts related to the behaviour of bats? Griffin and Galambos have carried out experiments with a large number of bats using a set of vertical 1-mm. wires only 30 cm. apart as a very difficult standard test. They find that normal bats strike the wires only 35 per cent of the times they fly through the grid. Either deafened or gagged bats, on the other hand, strike the wires an average of 65 per cent of times. This figure is found to be very near to the theoretical percentage of crashes to be expected on the assumption that they had no knowledge of the wires' existence.

It is of interest to note that, as in radar, an estimate of the *distance* of a reflecting surface is probably provided by the time taken for a pulse of vibrations to return to the bat. Exactly how an estimate is made of the *direction* in which the reflected waves return is not completely understood. What is clear, however, is that, as in ordinary sound localisation, a pair of ears is necessary. In this connection it has been found that bats deafened only in one ear strike the experimental grid as frequently as those deafened in both ears. Several theories of sound (and, for bats, supersonic wave) localisation have been in the field for many years. Three have much to commend them:

(*a*) The intensity-difference theory is based on the fact that there is a difference in the loudness of the vibrations reaching the two ears due to a shielding effect of the head. The difference is greatest when the source is in line with the two ears and zero when it is immediately in front or behind.

(*b*) The time difference theory depends on the time-lag in the arrival of pulses of sound at the two ears which occurs unless they are equidistant from the source.

(*c*) The phase-difference theory has its basis in the fact that, for a pair of ears each at a different distance from the source, each will be receiving at a given time a different part of the cycle of compressions and rarefactions of the air.

A discussion of the relative merits of these mechanisms would be out of place here, but to some extent they are not incompatible and each may play its part over a limited frequency range. The same difficulty in deciding the exact mechanism applies equally well to the case of ordinary sound localisation by human beings. In fact for bats the difficulty may be smaller on account of the pulsed nature of the signals. Localisation on the basis of time differences—in any case an attractive theory—is much more feasible for pulsed than for continuous signals.

ON CUTTING YOUR FINGER

By Michael Abercrombie

THE several billion cells which go to make a man live in a private world of their own, isolated from the larger world by his almost impermeable skin. Their world is the fluid medium which bathes them. This is not the blood but the tissue fluid which lies outside the blood-vessels in immediate contact with nearly all cells. Its composition is totally different from that of the aerial environment outside the skin; and if the cells are to survive, its composition can vary only within narrow limits. Physiology is in large part the study of ways in which the correct composition of the internal medium is maintained in the face of a very different outside world. The restricted permeability of the skin is one of these ways. A man, for instance, is very wet inside as compared with his normal surroundings, and he is helped to remain so by his skin, which is fairly waterproof when his sweat glands are not working (the unavoidable total leakage from a man's skin in ordinary circumstances is about 1 oz. of water per hour). Again, he is surrounded in daytime by ultra-violet light, which is very destructive to living cells, but it rarely passes through the outermost layer of his skin; when it does the result is painful sunburn. His environment teems with bacteria, many of which can multiply in his internal medium and poison his cells; but they cannot get through his undamaged skin.

In these and other ways the skin is a *passive* barrier. The skin also takes part in the *active* compensatory processes which correct any deviation from constancy on the part of the internal medium. For instance, while not impervious to heat, it can regulate its heat loss within limits. By changing the calibre of its superficial blood-vessels, varying amounts of warm blood from the interior of the body are brought close to the relatively cool atmosphere. By secreting sweat, the body is covered with a layer of water which evaporates into the relatively dry atmosphere, and evaporation withdraws heat from the skin. It thus provides one of the mechanisms by which variations of body temperature in mammals are corrected. The skin also, through its numerous sense-organs (see Le Gros Clark in *New Biology No. 1*), initiates many of the compensatory and defensive actions by which an animal maintains itself in being.

So much for the general importance of having a skin. A breach in its continuity obviously demands the immediate mobilisation of stopgap mechanisms to deal with the leakage of environment in and the leakage of animal out, and it also demands rapid permanent repair. In describing and analysing these processes we shall follow in slow motion the reaction to a very minor injury: a small superficial cut of a finger with a sharp knife. A more extensive injury than our simple example would involve numerous general reactions of the whole body, and we must in this article avoid entanglement in such interesting complications.

Structure of Skin. Skin is a composite structure (Fig. 1). It consists of a thin outer layer, the *epidermis,* which contributes its environment-proof characteristics; and the much thicker *dermis* beneath, which gives it mechanical strength.

The knife first cuts through the epidermis, a sheet of closely packed cells, forming a layer many cells deep. It is roughly 1/10 to 1/5 mm. thick on the back of the fingers and about five times thicker on the front. Only the inner part of the epidermis is living. The cells of this inner zone are about 1/70 mm. in linear dimension, and there will be ten thousand or more per square mm. of skin. These cells are actively multiplying. The new cells produced move up towards the surface, and as they go they die in a rather peculiar way. They become hornified, that is largely converted to a protein, *keratin* (the protein which makes up horns and hooves, hairs and feathers), which is chemically very resistant. When they finally reach the surface they are soon rubbed off and replaced from below. The superficial layer of the skin therefore consists of dead cells. It is this hornified zone which diminishes water loss, cuts out the ultra-violet, resists anything that pathogenic bacteria can do to it, and generally takes the rubs.

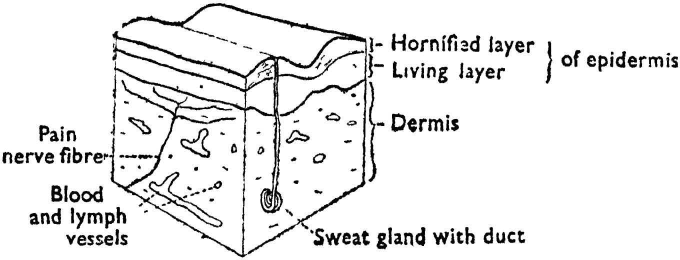

Fig. 1.—*A cube of skin, highly diagrammatic, to show some of the structures referred to in the text.*

Having penetrated the epidermis, injuring and destroying many of its cells on the way, the knife enters the *dermis,* a thicker layer of very different structure. Instead of cells closely packed as in the epidermis, its cells are sparsely scattered (about three-quarters of the volume of a human body consists of cells, the other quarter of intercellular material of various kinds, including tissue fluid which we mentioned at the beginning of this article. In the dermis the proportion of cells is unusually low). The intercellular space is largely taken up by tough bundles of protein fibrils arranged mainly parallel to the skin surface. Each protein fibril is about 1/10,000 mm. in diameter (as measured under the electron microscope), and a bundle may contain many thousands. The protein concerned is *collagen,* and it makes up about 60 per cent of the dry weight of skin. The epidermis, though chemically so resistant, is not mechanically very strong, and the ability of the skin to resist severe stretching depends mainly on its collagen fibres. Collagen is widespread in tissues throughout the body. It forms gelatin when it is boiled, and the collagen of skin when tanned is leather.

Our cut, however neat and clean, will damage or destroy many of the cells of the dermis. The scattered cells which lie between the collagen fibres are predominantly of two types, *macrophages* and *fibrocytes*. The importance of these in the response to injury we shall see shortly. Whether they have any rôle in uninjured skin we do not clearly know. But it has been found, by feeding animals with chemical compounds (amino-acids) marked by an isotopic element, that the collagen of tendon is not as inert as it had seemed to be. It is continually losing individual constituent atoms and replacing them by other atoms of the same kind, so that its chemical composition and microscopic appearance stay constant while its individual atoms change (the flame of a gas cooker, for instance, has the same property). The same, no doubt, applies to dermal collagen. This perpetual replacement is very possibly the work of near-by fibrocytes. Besides these cells the dermis also contains nerves, blood- and lymph-vessels, referred to later, and *elastic fibres*. These fibres are, like collagen fibres, non-cellular; but unlike collagen fibres, which do not give under tension until they break, elastic fibres stretch and rebound like india-rubber. Aided by a slight elasticity of the epidermis, and the fact that the skin is under a small degree of tension, they suffice to retract the edges of the wound, making it gape a little.

Pain. As the knife enters the dermis it passes through a tangle of fine nerve fibres which lies close under the epidermis. These nerve fibres end in the intercellular spaces of the dermis, or penetrate a short way into the epidermis and terminate there between the cells. When stimulated they transmit nerve impulses to the central nervous system, and when the impulses are relayed to the brain a sensation of pain results. They are very drastically stimulated by the knife which cuts them, and a volley of impulses reaches the brain in a small fraction of a second. These swiftly moving impulses may provoke from the central nervous system an immediate return volley of impulses down other nerve fibres which run to muscles of the arm. The contraction of these muscles jerks the wounded hand away. Such a reflex withdrawal is much less consistently obtained in the human arm than in the human leg. The arm, with its elaborate manipulative function in man, is under more flexible and complicated control from the brain than is the leg.

The instant jab is not the only pain produced by the entry of the knife. About a second later, it is followed by another wave of pain, this time of a rather more prolonged, burning kind. Attention may be too distracted to notice the two pains as separate, but they can be observed by gently pricking a finger or, better still, a toe. They form an interesting demonstration of different rates of conduction of impulses by nerve fibres. Speed of conduction depends on diameter of nerve fibre, and there are apparently two sets of pain nerve fibres in the skin, one large and one small. Both are practically simultaneously stimulated by the knife, but the slow impulses in the fine nerve fibres get left behind on their way to the central nervous system. The pains become more separated the farther the injury is from the central nervous system, and this fact makes a toe more useful experimental material than a finger. The discomfort of stubbing one can be relieved by a close study of the double nature of the pain.

The knife is now in and out, and the first reactions, of pain and reflex withdrawal, are over. Communication has been established between the inside of the animal and its environment. The contents of the animal will start to escape out of the various fluid spaces opened. Only the blood, however, has a copious enough flow to be lost rapidly in important amounts from a small wound.

Blood-clotting. The skin has a moderately rich blood-supply, confined entirely to the dermis. The epidermis is nourished by diffusion from the underlying blood-vessels, and it can be damaged, as by a superficial scratch, without blood-loss. Blood arrives in the skin from the heart through *arteries,* which are large-bore vessels with thick walls containing contractile muscle cells capable of altering the calibre of the vessel. The arteries divide up into ever more numerous and ever smaller branches, and eventually give rise to a very close network of *capillaries.* These are minute vessels about 1/100 mm. in diameter, the walls of which consist of a single layer of flattened cells. The capillaries join up into larger vessels, thin-walled *veins,* which conduct the blood away from the skin and back to the heart. It is through the capillaries and smaller veins that interchange between blood and tissues takes place. The smaller arteries (*arterioles*), with their muscular walls controlled mainly by the nervous system, have been compared to stop-cocks regulating the amount of blood which flows through the 'interchange' region, the capillaries and small veins. But capillaries and veins can also alter their calibre, the former by change of shape of the layer of cells constituting their walls, the latter by muscle cells like those of the arteries, but feebler.

There is a mechanism, blood-clotting, which rapidly puts a stop to the escape of blood from the wound. Blood-clotting is an intricate process of action and counter-action which because of its complexity has been troublesome to investigate. The complexity is understandable, since it is vital to the organism that blood should never fail to clot in a wound, but should never clot in the general circulation. Concerning the mechanism of the process we need only say that small amounts of two proteins normally circulate dissolved in the blood, *prothrombin* and *fibrinogen.* Under the stimulus of the wound, prothrombin is locally converted into an enzyme, *thrombin,* and the thrombin then converts the soluble fibrinogen into a meshwork of insoluble *fibrin.* The fibrinogen forms less than 0·5 per cent of the blood by weight, yet the fibrin, its insoluble product, forms such an extremely close tangle of delicate needle-like fibrils that all the rest of the blood, both cells and fluid, is held in its mesh, and the whole takes on the consistency of a jelly. The wound is plugged by this jelly and the outflow of blood therefore ceases.

The conversion of prothrombin to thrombin is the essential step in clotting, and this is the work of an activating substance produced in the wound. The source and nature of the activating substance is not yet fully determined. It comes in part directly from injured cells; an extract of crushed tissue is therefore very effective in clotting blood. It comes also from minute bodies (by origin probably fragments of cells) called *blood platelets,* which normally circulate in the blood. Somehow, when the blood comes in contact with tissues other than the lining of the blood vessels, as in a cut, the platelets disintegrate and yield an activating substance which converts prothrombin to thrombin.

The clotting mechanism is highly effective, and very rarely lets a person down. Sufferers from the hereditary disease *hæmophilia* may bleed dangerously from a minor injury, apparently because for reasons unknown they form thrombin only very slowly after injury. Occasionally, also, severe bleeding may occur as a result of deficiency of prothrombin, since its formation by the liver depends on an adequate intake of a vitamin (K) which is not always assured.

Our small wound, therefore, becomes plugged within a few minutes by a blood-clot firmly attached to the tissues around it. If it is left exposed to the air the surface of the clot soon dries, forming a scab which temporarily proofs the wound. The inner part of the clot restores physical continuity between the sides of the wound and thus forms a scaffolding for subsequent reconstruction.

So much for the leakage of the animal out through the wound. What about the leakage of environment in?

Animals and Bacteria. Because bacteria may multiply within the body, the minutest wound can introduce a lethal dose. From the point of view of skin injury they are the most dangerous element of an animal's environment.

It must not be thought that in the absence of injury the interior of the body is quite devoid of bacteria. The alimentary canal, including the mouth, nose and throat, but excluding the stomach (whose acidity makes it antiseptic) contains myriads of them. A quarter of the weight of fæces is bacteria. The question whether other parts of the body, and especially the muscles, normally contain bacteria is one which has interested the butchery trade. It appears that the muscles of some mammals do normally contain a small number of bacteria, probably a transient population which is being continually recruited from the intestines and continually destroyed in the blood-system. This is true, it seems, of human beings. But these bacteria are so few that for practical purposes the inside of a healthy man (excluding from consideration the gut) is free of bacteria, while his surroundings are full of them.

We need to go no further into the outer world than the surface of the skin to find bacteria in considerable numbers. But the bacterial population of the skin surface is rarely very large, and only a few species are permanent residents. This is because of a little-understood antiseptic action of normal skin, perhaps due to certain fatty acids normally found there. The efficiency of this natural antisepsis is incidentally reduced by dirt on the skin. There are some thousands of resident bacteria per square inch of human skin (fewer on clothed parts of the body than on exposed parts, and varying much from person to person). No amount of scrubbing or disinfection will rid the skin of these bacteria entirely, probably because some are protected by living deep in the hair roots and sebaceous glands. But the body is not in such a state of siege as these figures suggest, since most of the resident bacteria are not dangerous when they get inside the body—they are not *pathogenic*. They are harmless organisms sharing the same skin as ourselves. Neither probably are they of any value to us, as are some of the intestinal bacteria which synthesise part of our vitamin supply (e.g. vitamin K referred to above). But roughly 10 to 20 per cent of people carry a real pathogen on their skin—*Staphylococcus pyogenes*, the bacterium which produces boils, and commonly the first pathogen to get into the wounds of the skin. Other pathogenic bacteria may be transiently present on normal skin, but they cannot persist long against the natural antisepsis.

The knife, therefore, cannot help but carry in bacteria, some of which may be pathogens, from the skin. But the victim's skin is not the only possible source of infection. Careless first-aid may introduce the inhabitants of someone else's skin. Noses and throats of the victim and of his sympathisers harbour *Staphylococcus* much more often than their skin does, and they frequently carry *Streptococcus pyogenes* too, another important pathogenic invader. Not only sneezing and coughing but also mere talking will spray a number of these into the air; and they make an inexhaustible reservoir for contamination of hands and handkerchiefs. Furthermore, many pathogenic bacteria when not in or on their human hosts can survive considerable periods in floating or settled dust, especially if they are not exposed too much to the faintly antiseptic action of daylight. Just as we are horrified by the casual attitude to sewage disposal of a century ago, our descendants will be disgusted by the indifferent way we share our buildings with bacterial parasites.

Inflammation. The defence mechanism which has developed during the evolution of vertebrates to cope with invading bacteria is the inflammatory reaction. The characteristics of inflammation were described nineteen hundred years ago as 'redness, heat, swelling and pain' of the affected part, and these headings still provide a useful framework for discussion. Before long these familiar phenomena will appear in the immediate neighbourhood of our cut, and we must proceed to analyse what is at the back of them.

Redness and Heat. The redness and heat are due to an increase in calibre of the blood-vessels around the wound. As a result of this dilation of vessels there is at any moment more blood than usual in the inflamed skin, and the skin colour consequently deepens. The small veins and capillaries just below the epidermis are mainly responsible; they present a much greater surface than do the arterioles. The dilation of the arterioles (the 'stopcocks') makes the skin hot, since the extra incoming blood carries more heat from the inside of the body, which is some 10° C. hotter than the normal skin of the hand. (By arteriolar expansion, likewise, the normal skin cools the body when it gets too hot.)

How is the damage from the knife translated into blood-vessel dilation? We owe most of our important knowledge of the process to Sir Thomas Lewis, a scientist who had an unusual genius for simple and telling experiment combined with complicated and subtle argument. Experimenting mainly on himself or his collaborators, he investigated milder degrees of skin injury than the cut we are discussing. Repeated firm strokes, made with a bluntly pointed instrument and carefully superimposed, or a scratch which need tear the epidermis only, produce, as the reader can almost painlessly verify, a characteristic 'triple response.' It has the following three components: (1) within a few seconds a reddening confined to the narrow injured region, often surrounded by a zone of transient blanching; (2) shortly afterwards a surrounding 'flare' of red which may be an inch or so wide; (3) later still a weal in the place of the first red reaction. The triple response can conveniently be elicited from the inner side of the forearm.

We can unfortunately follow Lewis's ingenious analysis of the triple response only in outline. He showed that reaction (1) is due to a dilation of capillaries and veins occurring in response to a chemical substance released by injured cells. He inferred the existence of a chemical stimulus from the fact that the dilation shows unusual persistence, and a tendency to spread, when the blood-supply to the arm is cut off by a tightly constricting band. This is reasonably explained by supposing that a dilating substance is normally carried away by the circulation, but hangs around and diffuses outwards when there is no circulation. The peripheral blanching which accompanies the local red reaction is due to constriction of vessels as a direct response to mechanical stretching at the time of injury.

Reaction (2), the widespread flare, is the result primarily of a dilation of arterioles. A chemical stimulus, presumably the same as that concerned in reaction (1), sets the flare going. But experiments made after the nerves to the injured area have been cut show that the chemical stimulus does not act immediately on the arterioles, but *via* nerve fibres. These nerve fibres directly connect the injured spot with the walls of surrounding arterioles. Such an arrangement of nerve fibres might seem entirely natural, but it is highly exceptional. In almost all other reactions the nerve impulses have to go first into the central nervous system, where they can be co-ordinated with other impulses, and then out again along other nerve fibres to produce their response (like the impulses concerned in reflex withdrawal of the hand. See also J. Z. Young in *New Biology No. 1*). The direct connection (which is called an axon-reflex), which Lewis found to be responsible for the flare is probably made by terminal branches of ordinary nerve fibres. Some branches of each nerve fibre end on arteriole muscles, others (stimulable by the dilator substance) end elsewhere in the dermis.

What is the dilator substance? Because the introduction of minute amounts of *histamine* (a tiny drop at a dilution of 1 part in half a million of water) causes the whole triple response, Lewis thought that the dilator (and also the causative agent of the weal, which we shall shortly discuss) was closely related to histamine, and he called it 'H-substance.' But since free histamine or a related substance has not yet been satisfactorily demonstrated in the region of the simple triple response which Lewis himself studied, nor in some other examples of tissues displaying the dilation, the status of 'H-substance' is still uncertain.

Our cut is more complicated than a simple triple response. The escaping blood will, for instance, at first remove and dilute any dilator substances. Nevertheless it is very likely that Lewis's analysis, except perhaps for his identification of the kind of chemical involved, applies to the early stages of blood-vessel dilation around a cut. We may suppose that the knife, by injuring epidermal and dermal cells, causes a substance (or substances) to be released which directly dilates the capillaries and small veins and arterioles in the immediate vicinity, and by stimulation of nerves, dilates a surrounding zone of arterioles (a relatively narrow zone on a finger). But whether the same process is responsible for the continued dilation which keeps the margin of the cut reddened for several days is doubtful. About that we know practically nothing.

Swelling. The inflammatory swelling (corresponding to reaction (3), the wealing of Lewis's triple response) might seem to be due, like the redness and heat, to the increased amount of blood in the vessels. Actually a more important cause is the appearance of extra tissue fluid *outside* the blood-vessels in the crannies around and between cells and collagen bundles. This fluid comes from the blood in the capillaries, and it will therefore not appear if the blood-supply to the damaged region is cut off. It escapes from the capillaries because of an increased permeability of the walls of these vessels in the inflamed region: increased permeability not to water, however, but to large molecules such as proteins.

The escape of proteins from the capillaries is accompanied by an escape of water, because of the peculiar way that fluid normally stays within blood-vessels. The water which makes up 90 per cent of blood plasma is not held within the blood-system by the existence of waterproof vessels; on the contrary, water can pass freely through capillary walls. In rabbits, experiments with heavy water have shown that 70 per cent of the plasma water is exchanged with tissue water per minute, and this exchange is an essential part of the mechanism by which food is carried from blood to tissues. It might be supposed that the effect of pumping blood through a system of tubes as leaky as those of the blood-system would simply be to pump fluid out into the tissues; but the necessary volume of water is firmly held within the blood-system by osmotic pressure exerted by proteins, dissolved in the blood plasma. To these proteins the capillary wall is normally almost impermeable. The tendency of the heart to pump water through the capillary walls is normally balanced by the tendency of the plasma proteins to hold water in. Actually in some parts of the capillary system the balance is tipped one way ; in other parts it is tipped the other. The net result, however, is that the blood-system loses very little water to the tissues. In inflammation an increased permeability of the capillaries to large molecules can be easily demonstrated by injecting into a vein a non-poisonous dye which, because of its large particles, is normally held within the blood-system just as the proteins are. A commonly used dye is trypan blue. An inflamed region rapidly becomes intensely stained through diffusion of the dye out from its capillaries. In the same way the blood proteins must be leaking out, and the intercellular fluid of an inflamed region can be shown by chemical analysis to be unusually rich in proteins. The escaped proteins then compete with the blood proteins for water, and extra water passes into the tissues.

What causes the increased permeability of the capillaries to large particles? Lewis considered that it was due to the action of 'H-substance' on capillary walls. A more recent series of researches by Menkin of Harvard incriminates a substance quite unrelated to histamine. Menkin carried out a laborious analysis of inflammatory fluid, testing each fraction for its permeability-promoting activity by injecting it into the skin of a rabbit, which also received a dose of intravenous trypan blue for the reason just stated. The size of the stained patch was compared with that resulting from neighbouring injections of other fractions, and (as control) of the solvent in which these fractions are dissolved. His fractionation culminated in a highly purified substance, which he called *leucotaxine*, It is a polypeptide, i.e. a product of the partial breakdown of protein. It produces intensely increased permeability in very high dilutions (one part in 100,000 of water) and is in this respect far more active than histamine, though this substance does increase permeability a little.

Living things are complicated and fickle, and when one living thing investigates another, error has opportunities. It is well, therefore, that results as striking as those of Menkin should be confirmed and extended in other laboratories. Duthie and Chain in Oxford have in fact substantiated much of Menkin's story. The most reasonable hypothesis is, therefore, that leucotaxine is released from the killed and damaged cells of the injured skin we are considering, and is mainly responsible for the escape of fluid from nearby undamaged capillaries, an escape which starts within a few minutes of the cut and progresses till it produces visible swelling.

Clearly, fluid does not go on accumulating around the injured region. This is, no doubt, partly because the increased pressure in the swollen tissue begins to oppose the entry of any more fluid, and because sooner or later the capillary permeability reverts to normal; but it is also because the fluid is carried away by a system of vessels which we have not so far mentioned, the *lymphatic system*. Lymph-vessels begin blindly in the dermis as a fine network of tubes, little bigger than a blood capillary in diameter, with a delicate wall one cell thick. These tiny vessels connect up with larger vessels, just as does the system of veins, and finally drain back into the blood-system through a few major connections with veins in the chest. On the course of the large lymph-vessels are small rounded swellings called *lymph nodes*, whose importance we shall see in a moment. In a normal tissue the minute blindly ending lymph-vessels, unlike blood capillaries, are easily permeable to proteins and indeed to quite large particles. They act like sewers, taking up a certain amount of the fluid which leaks through the blood capillary walls, together with any debris that may appear in the tissue spaces, and transporting this fluid, which is lymph, back into the blood-stream.

In the inflamed region of our cut the excess of tissue fluid is carried away by the lymph-vessels, which become even more permeable, so that bacteria can pass through their walls. It is *via* the lymphatic system that bacteria will spread from the wound; they can rarely gain access directly to the blood-stream because the flow of fluid through the blood-vessel walls is against them. As they travel along in the lymph, they arrive before long at the lymph nodes which filter out and destroy bacteria, becoming themselves inflamed in the process. If your cut finger is badly infected with bacteria, you may soon find 'swollen glands,' which are inflamed lymph nodes, in your armpit. If the nodes are ineffective, bacteria will reach the blood circulation, where, though they will meet other powerful defences, they may quickly become a serious menace to life.

Does the exudation of fluid from the capillaries into the tissue spaces help to defend the animal against invading bacteria? The traditional view, for which there is not much experimental evidence, is that it does so in the following ways. It brings into the tissue spaces increased amounts of the powerful natural antiseptics called *antibodies* which circulate in the blood, though some are present in normal tissue fluid. And it dilutes any poisons produced by bacteria, and helps to sweep them away through the lymphatics, so that widespread mechanisms can oppose them. This antiseptic washing down of the tissues may be important. But flushing the tissues out would obviously be a dangerous procedure if it also broadcast virulent bacteria throughout the body. In fact, however, while some escape through lymph-vessels is usual, most bacteria as a rule remain effectively localised around the cut. This seems to be partly because some of the antibodies of the tissue fluid make bacteria stick to each other and to the tissues in clumps which are not easily shifted. Partly it is because in severe infection with much local damage the fibrinogen which leaves the capillaries along with the other blood proteins clots in the tissues, trapping bacteria and plugging lymph-vessels.

Bacteria, then, are to some extent held at the place where they were introduced, especially if they produce much local damage; and to some extent they escape at least as far as the near-by lymph nodes. Their escape is not necessarily a disadvantage to the organism, since it permits the elaboration of antibodies. Antibodies are highly specific. Each sort of antibody is made only in the presence of, and reacts only with, one particular foreign substance. The escape of bacteria from a local injury allows the organs which make antibodies, of which the lymph nodes may be very important, to come into contact with the invaders, and to prepare specific antibodies which kill or clump the bacteria and make their poisonous products (toxins) innocuous. Once made, the antibodies persist for a time in the body, though in diminishing concentration. They are thus available to deal with the next invasion, which in its turn will stimulate a new outburst of antibody production.

Movement of the injured limb is liable to encourage spread of bacteria by promoting lymph flow. This is because the ordinary limb muscles, as they work, squeeze the lymph along in its vessels, which have valves ensuring that the flow is in one direction only. But the body is to some extent protected against such bacterial spread, because an injured limb, especially if severely infected, is normally kept fairly still, since it is painful to move it.

White Cells. It is not only proteins which escape from inflamed capillaries. White cells (leucocytes), which normally circulate in the blood-stream, also traverse the walls of veins and capillaries in the damaged region (they do not leave the vessels of normal dermis in appreciable numbers). They are perhaps the most important part of the local defence mechanism against bacteria, but because they are microscopically small their presence was overlooked in the classical description of inflammation. The importance of these white cells, and especially of the most numerous of them called *polymorphs,* is that they devour or destroy any bacteria they may come across. The number of polymorphs in an animal's blood can be experimentally reduced almost to zero by poisoning it with benzene. Even if such an animal, depleted of its polymorphs, is experimentally well protected by antibodies, it is incapable of preventing the multiplication of locally injected pathogens, i.e. bacteria, and an ultimate fatal invasion of the whole body.

The mechanism by which white cells leave the bloodstream and accumulate in an inflamed area is as follows: the blood, unusually viscous because of loss of fluid, flows slowly in the expanded vessels of the damaged region. The lining of the veins and capillaries there becomes sticky for white cells, and polymorphs consequently become attached to the inside of the vessel walls in considerable numbers. Soon, but usually not before an hour or two after the injury, the attached polymorphs push their way between the lining cells of the vessel walls and so out into the tissue spaces. This penetration of the wall seems to be mainly due to an active movement on the part of the polymorphs. But immobile bodies such as red blood corpuscles or injected carbon particles will also pass out of an inflamed capillary. Perhaps the intercellular material which binds the capillary cells together is like quicksand, i.e. it liquefies under mechanical disturbance. Particles stuck to the cement and agitated by the blood-stream might then be pushed through under the pressure of the blood. Before long the tissue around the cut becomes infiltrated with migrating polymorphs, which engulf and digest the debris of the wound damage (they do not touch living cells) and the bacteria which have inevitably got into the wound.

Menkin has shown that the migration of polymorphs is probably another effect of leucotaxine. This substance has a powerful attractive influence on polymorphs. The attractiveness can be readily shown in artificial conditions outside the body by placing two tiny glass tubes in a drop of serum containing leucocytes. One tube contains leucotaxin absorbed in an inert substance, the other contains the inert substance alone. It is found that the polymorphs pour into the leucotaxine-containing tube, while the other tube remains empty. No other purified substance has anything like the attractive power of leucotaxine. Histamine is quite ineffective (and leucocytes do not accumulate in a simple 'triple response').

Besides the invasion of the injured region by polymorphs from the blood, other cells also take part in the phagocytosis which helps to rid the area of invading bacteria. Most of these cells do not come from the blood; they are already on the spot. They are the *macrophages*, and they make up about a quarter of the total cell population of the normal dermis. They are widely distributed in all tissues of the body. In liver, spleen and bone marrow they are in contact with the blood-stream. They remove from it with extraordinary effectiveness all kinds of foreign bodies, such as bacteria which have escaped the lymph nodes, or malaria parasites (see Johnson in *New Biology No. 1*, where these macrophages are given their collective name of reticulo-endothelial system). The filter mechanism of the lymph nodes itself consists of macrophages. Macrophages can easily be distinguished from other tissue cells by the fact that when trypan blue is injected into the living animal they take up large amounts of the dye in the form of deeply stained granules. Other cells remain substantially unstained. In the neighbourhood of an injury the macrophages of the dermis round up, swell, multiply and migrate towards the damage. (Another chemical from damaged cells, choline, has lately been suggested as responsible for macrophage mobilisation, but the work is as yet unconfirmed.) There they ingest bacteria and above all cell debris. The joint activity of scavenging polymorphs and macrophages cleans up the whole region. Their work done, most of these cells degenerate or leave the inflamed area by the lymph-vessels.

Tenderness. The fourth classical characteristic of inflammation is pain; not the immediate pain of injury, but the long-continued subsequent pain, or, more usually, tenderness, a condition which takes an appreciable time to develop after the initial injury. Inflamed skin is very tender: stimuli which would normally be ineffective, such as a very mild degree of warmth or tension or friction, excite its pain nerves. Indeed, the nerves may become so sensitive that body temperature is enough to excite them and continuous pain results; or the slight tension produced by a beating artery near by stimulates them and gives rise to a throbbing pain. This tenderness extends out a little way from the place of injury, and Lewis has supposed that it is due to the continuous liberation of a substance from injured cells, which makes the pain nerves more susceptible than usual to stimulation. We have no clear information as to what the substance is.

Tenderness results in a relative immobilisation of the part (important, as we saw above, in relation to the spread of infection through the lymph channels) and the avoidance of further bacterial infection by contact with contaminated objects.

Pus. We have now completed our description of the main features of the inflammatory reaction which follows a small cut. The whole process reaches its maximum some hours after the original injury and features of it persist for several days. Its maximum intensity is, however, short-lived, provided there is no further injury to the damaged skin. If injury is continuous, then inflammation becomes severe and persistent; and there appears, as a result of extensive cell destruction, a rather common complication, to which we must briefly refer: the formation of *pus*.

The continuous injury which produces pus is in most instances the result of continued *bacterial* irritation, but it can be produced experimentally in the entire absence of bacteria by the persistent presence of damaging chemicals. This pus is dead tissue liquefied by digestion, containing masses of dead polymorphs. All cells, and especially the polymorphs, contain enzymes which digest proteins. These enzymes are responsible for the self-dissolution of cells when they die. The death of large numbers of polymorphs in a severe local infection is doubtless caused by poisonous bacterial products, and the disintegration of these cells liberates their digestive enzymes into the surroundings. The dead area, including intercellular material, is then rapidly liquefied.

Three general points about the inflammatory reaction need emphasis. Firstly, we have treated the process throughout as a defence mechanism against bacterial invasion. But the mechanism is *not necessarily set going by bacteria.* It can be set going by anything which causes tissue damage: in the case we are discussing, by the mechanical injury of a cut. Severity of inflammation depends on the amount of tissue damage, and it becomes particularly well marked when the initial damage is supplemented and continued by bacterial invasion. But the animal as it were assumes, quite rightly, that skin damage will introduce dangerous bacteria, and reacts immediately without waiting for the bacteria to make themselves felt.

Secondly, the inflammatory reaction is a complicated but well-integrated one. It is integrated apparently because it depends on the simultaneous release from injured cells of a group of active chemical substances, each of which evokes part of the reaction (see Fig. 2). We are certainly only at the beginning of the list of these activators. Menkin is at present adding a new one, 'necrosin,' which apparently extends the zone of injury caused by the initial stimulus, damaging surrounding cells. Work done during the war on burn injuries has indicated that

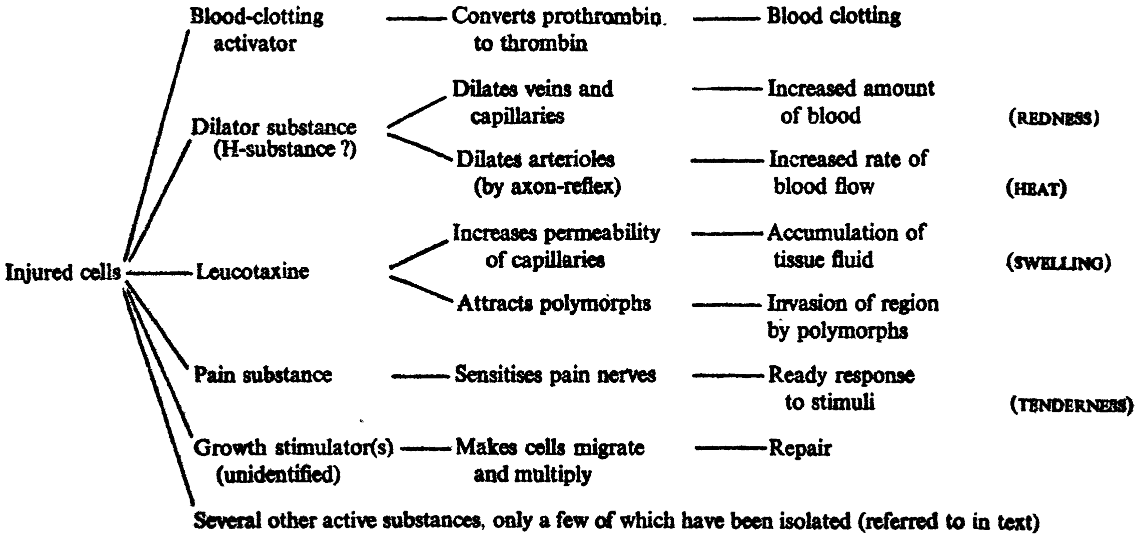
Injured cells
Blood-clotting activator
Converts prothrombin to thrombin
Blood clotting
Dilator substance (H-substance ?)
Dilates veins and capillaries
Increased amount of blood
(REDNESS)
Dilates arterioles (by axon-reflex)
Increased rate of blood flow
(HEAT)
Leucotaxine
Increases permeability of capillaries
Accumulation of tissue fluid
(SWELLING)
Attracts polymorphs
Invasion of region by polymorphs
Pain substance
Sensitises pain nerves
Ready response to stimuli
(TENDERNESS)
Growth stimulator(s) (unidentified)
Makes cells migrate and multiply
Repair
Several other active substances, only a few of which have been isolated (referred to in text)

Fig. 2.—Diagram of the response to injury, showing its origin from a group of activating substances produced by injured cells.

damaged cells may release a protein-splitting enzyme (note that leucotaxine is a product of protein-splitting). These and other lines will converge and diverge on to many new activators. But though our knowledge is highly incomplete, the way the integration of the inflammatory reaction is achieved is now clear.

Thirdly, we have confined ourselves for simplicity to a very minor injury of the skin, but the local reaction to injury has fundamental similarities everywhere in the body. Apparently all parts of the body contain cells capable when injured or killed of producing the various stimulating substances. Appendicitis is, for instance, a typical inflammation of part of the intestine. Any disease whose name ends in *itis* involves an inflammatory reaction. There are, of course, differences from place to place (the axon-reflex dilation of arterioles, for instance, is absent from internal organs) and also according to the nature of the injurious agent. Nevertheless, the familiar outline of the reaction to injury can everywhere be discerned.

The General Reaction. We have already indicated one important way in which the rest of the organism can be affected by a local injury: *via* the pain nerves. As a result at least the organism's future activities with a sharp knife are likely to be circumscribed. The rest of the body can be affected in other ways, which are evident when tissue damage is widespread. For instance, the loss of fluid from the blood through the permeable capillaries of extensive burns or crushes may be so great that the circulation eventually fails ('shock'). The absorption into blood or lymph of products of injured cells is another cause of a general reaction. But since this likewise concerns only severe injuries, I will confine myself to mentioning that Menkin has obtained active proteins from inflamed regions. One of these, when it gets into the general circulation, causes the liberation of extra polymorphs from the bone marrow, their place of manufacture, into the blood-stream, so that the blood becomes unusually rich in these cells. Another sends up the general body temperature.

Repair. To complete the history of our injury I must briefly refer to the process by which the finger heals, and thus once more achieves isolation from its environment. I have chosen to pay more attention in this article to the emergency measures so far discussed, because what we know of the process of repair makes much less of a coherent story. Even the straightforward description of what happens is still incomplete.

The cellular activities which ultimately lead to repair do not wait until inflammation has subsided. They start almost immediately around the region of injury. The closing of the wound may be delayed or the wound may be enlarged as a result of further damage done by invading bacteria, but, nevertheless, at the margin of the region of injury incipient repair processes such as cell multiplication will usually be going on.

The connective tissue cells of the dermis are the first to react. We have mentioned the macrophages, which are scavengers. The other important cells in the dermis are the *fibrocytes.* Around the wound fibrocytes swell and migrate towards the cut within a few hours of wounding and soon start to multiply. When they reach the fibrin clot which fills the gap the fibrocytes make their way through it. Polymorphs and macrophages will already have colonised it.

Along with the fibrocytes new blood capillaries also invade the blood clot. They are formed quite simply as hollow sprouts from the remaining blood capillaries around the wound. Their progress has been watched by an ingenious technique of microscopical observation of the living animal. The skin is removed from both sides of a rabbit's ear and replaced by sheets of perspex and mica, which are clamped in place. A thin transparent sheet of tissue is then available for microscopical examination over prolonged periods, and the budding of capillaries and the migration of many other cellular components of the tissue have been watched as they occur.

The blood clot is thus peopled with cells, but the skin has not recovered its full protective rôle, which depends on the restoration of an intact epidermis, by outgrowth of the original epidermis from the margins of the wound. Epidermis will hardly grow at all through the substance of a blood clot. It requires a solid *surface* over which to spread itself. In the wound which we are considering the hard superficial scab is soon separated from the mass of underlying soft clot by a shallow fluid-filled space, as the result of digestion by invading polymorphs. It is over the surface of the underlying clot, hidden by the scab, that the epidermis spreads in from the margins of the wound. It advances at very roughly ½ mm. per day. The sheet of living cells of the old epidermis seems to flow over the wound, almost like a viscous fluid. As epidermal cells come in contact with the upper surface of the new tissue which the blood clot has become, they adhere to it, and further epidermal cells then roll over them from above. The flow continues until the whole wound is covered by a relatively thin sheet of cells. The lower layer of the epidermis normally undergoes continual multiplication, as we saw above, and the effect of a wound is to speed this up. This increased multiplication in the epidermis builds the thin sheet of tissue, which first covers the wound, into epidermis of normal thickness. Not only is the normal thickness replaced, but, at least with a small wound, all details of structure recur. Nature works on the side of the law, ensuring that the surface pattern of the finger epidermis, which is responsible for finger prints, is replaced in every detail, unless severe destruction of the underlying connective tissue has occurred.

With the covering of the wound no more bacteria can enter. Epidermis is in fact the best antiseptic dressing possible for a wound. But though the wound is now covered, it would not long remain so if new collagen were not laid down beneath the epidermis, giving tensile strength to the new skin. This collagen is formed by the invading fibrocytes. It replaces the blood clot into which these cells have migrated, the fibrin and red blood-cells of the original clot being removed within about a week of wounding. The collagen fibrils first appear between the fibrocytes about four to five days after wounding. They gradually increase in size and in number until after fourteen days they are very like those of normal skin. Correspondingly the tensile strength of an incised wound rises from almost zero at four days to that of normal skin at fourteen days.

One of the few things that is known about the process of collagen formation is that an adequate supply of vitamin C is essential. Several investigators have recently proved this by experiments on themselves. An American worker, Crandon, endured for seven months a diet completely devoid of vitamin C. Towards the end of this time he had wounds made in himself and the tissues subsequently removed for histological study. The epidermis covered such wounds normally, but beneath there was a total absence of collagen. The collagen was rapidly laid down when he took large doses of vitamin C. Naturally this discovery is of importance in surgery, since those who have had a long period of malnutrition may fail to develop sufficient tensile strength in the scar to hold an operation wound together.

One respect in which a wound may fail to return to normal particularly concerns collagen formation. This is the appearance of a permanent white scar in the place of the original wound. The whiteness is due to excess collagen and a relatively poor supply of blood-vessels.

The epidermis is also thin and abnormal. The appearance of a scar is apparently related to the depth of the wound. Recent work suggests that there is some property of the more superficial part of the dermis which prevents scarring. When this superficial part is destroyed healing starts normally, but in its later stages turns to scar-formation.

To complete the restoration of normal skin several other components must be reformed, but these we will merely mention. Nerves reinvade the new tissue by sprouting from their cut surfaces. Lymphatic vessels regenerate, probably like blood capillaries, but later. Elastic fibres are very slow to reappear.

That is a very brief description of the processes involved in healing a skin wound. What controls them so that the end-product is normal skin? We have hardly the faintest idea. But the suspicion that products of injured cells are once more involved, at least in initiating cellular migration and multiplication, is likely to be justified. Tissue-culture work has shown that extracts of mashed-up tissues are very potent promoters of migration and multiplication. But we are very far from the satisfactory situation of botanists, who have seen the chemical identification of a wound hormone responsible for initiating repair in plants. A reliable and simple method has yet to be devised for testing the effect of various substances on the several components of the repair process in animals, as easy to use as the trypan-blue test for capillary permeability and the test for leucocyte attraction mentioned above. But perhaps our ignorance is excusable. At present the agent which most seriously delays and impairs healing is bacterial infection. The greatest contribution to wound healing at the moment is therefore improved antisepsis. When infection is no longer a constant menace to human wounds, the prevention of scarring and the speeding of epidermal growth through application of knowledge of the repair processes will become of immediate importance.

FURTHER READING

For a more detailed account of the structures referred to, and of their repair after injury, see W. E. Le Gros Clark's *The Tissues of the Body*. 2nd Edition. Oxford (1945).

The work of Sir Thomas Lewis can be followed up in his books: *The Blood-vessels of the Human Skin and Their Responses*. London (1927) ; and *Pain*. New York (1942).

The work of Valy Menkin is summarised in his *Dynamics of Inflammation*. New York (1940).

Valuable but technical sources of recent information are two numbers of the *British Medical Bulletin* (published by the British Council). Vol. 3 (1945): Nos. 4-5 on Injury and Repair, and Nos. 7-8 on Skin.

The following articles in *New Biology No. 1* are referred to in the text:
W. E. Le Gros Clark. 'The Anatomical Basis of Sensory Experience.'
J. Z. Young. 'The Functions of the Central Nervous System.'
M. L. Johnson. 'Malaria, Mosquitoes and Man.'

GLOSSARY

Algæ. Non-flowering plants, mostly aquatic, e.g. seaweeds, of which there are at least four groups, the green, blue-green, red and brown algæ. The green frothy scum often seen in ditches usually consists of green algæ, and most of the common seaweeds are brown algæ.

Alimentary Canal. The tube, leading from mouth to anus *via* œsophagus, stomach, and intestine, into which food is taken and in which food is digested.

Amino-Acid. *See* Protein.

Amphibia. A class of cold-blooded vertebrates in which the skin is soft and moist. The eggs are usually laid in water and the young pass through an aquatic tadpole stage. Frogs and newts belong to this class.

Anthelmintics. Poisons used to kill parasitic worms. The name Helminthes is sometimes used collectively for several groups of worms, of which the *Nematodes* are one.

Antibody. A protein formed in the body in response to the introduction of certain substances normally foreign to the body, including bacteria and their poisonous products. The antibody combines with the foreign substance, and, in the case of bacteria and their products, makes it harmless. It is uncertain where antibodies are formed. Once formed, they are found mainly in the blood, where they continue to circulate for a varying time after the initial stimulus to their formation has disappeared, so that a single infection with disease-producing bacteria or viruses may result in prolonged protection against that particular disease (immunity). In vaccination antibodies are artificially stimulated by injecting harmless forms of a disease-producing bacterium or virus.

Basal Metabolic Rate. The rate of energy expenditure of an animal at rest.

Blood. Consists of an almost colourless fluid called *plasma* in which are suspended large numbers of minute *red blood corpuscles* (about 5,000,000 per cubic mm.), and a smaller number of *white cells* (about 6,000 per cubic mm.). Plasma is 90 per cent water, the rest being dissolved proteins, salts and small amounts of innumerable organic compounds. Red blood corpuscles are discs of about 1/130-mm. diameter. White cells are spherical and rather larger.

Cell. Both animals and plants are built up of microscopic units called cells, stuck together and supported by intercellular material. Cells are of very various form and function, but they all have certain characteristics in common: (*a*) They are bounded by a membrane which allows some substances to pass through, but not others. (*b*) They contain one or sometimes several nuclei (each of which contains a set of the genes, or hereditary factors, which the organism has received from its parents). (*c*) Inside them go on most of the vital processes—essentially the synthesis of new material, and the destruction of other substances which liberate energy. Every animal and plant reproduced sexually starts life as a single cell (formed by fusion of a male and a female cell). This cell divides into two, and by continuous doubling the adult's millions of cells are formed.

Central Nervous System. Complicated behaviour by a complicated organism requires a central co-ordinating system. In the majority of animals, therefore, there is a central nervous system into which almost all impulses from the sense organs come and out of which almost all impulses to the muscles and glands go, so that it is in a position to organise all nervous activity.

CEPHALOPODA. The order of molluscs to which the octopus and squid belong. They are characterised by the possession of a ring of sucker-bearing tentacles round the mouth.

CRUSTACEA. A class of animals, mostly aquatic, characterised by a hard, jointed, external skeleton, often containing a deposition of calcium carbonate. Common examples are crabs, lobsters, shrimps and woodlice.

DINOSAURS. A group of reptiles which flourished in the Jurassic and Cretaceous periods (about 150 million years ago) and then became extinct. Many of them reached very large sizes.

ENZYME. Substance produced by living organisms which activates a chemical process. Enzymes are responsible for the processes of synthesis and destruction characteristic of living matter, which occur inside cells. There are many different sorts of enzyme, and each activates only one specific kind of chemical reaction. During the reaction the enzyme is not used up, so that a minute amount of enzyme can change a large amount of reactant. Enzymes are proteins or closely associated with proteins.

FATTY ACID. Ordinary fats are made up of fatty acids combined with glycerol.

FUNGUS. Simply organised plant lacking the green pigment characteristic of most other plants and obtaining its food from dead or living animal or plant matter, e.g. yeasts, moulds, toadstools.

HÆMOGLOBIN. The red colouring matter in vertebrate blood. Hæmoglobin has the property of combining reversibly with oxygen. In the lungs it becomes loaded with oxygen which it later gives off to the tissues as it is carried round the body in the circulating blood. Hæmoglobin also occurs in mammalian muscles where it acts as a go-between, taking oxygen from the blood and passing it on for use by the muscle cells.

HYDROGENATION. The alteration of the structure of a molecule by adding extra hydrogen. Oils are 'hardened' and converted to fats by adding hydrogen under slight pressure in the presence of finely divided nickel.

ICHTHYOSAURS. A group of extinct reptiles which lived about 150 million years ago. They were completely aquatic and swam with side-to-side strokes of the tail, and the limbs were reduced to small paddles. They did not lay eggs, but the young were born at an advanced stage of development.

IMPULSE. The 'message' which is conducted along a nerve fibre. It is a travelling electrical disturbance which moves along the nerve fibre at between 1 and 100 yards per second (speed according to nerve-fibre diameter).

ISOTOPE. The atoms of most chemical elements are not all alike, but are of a few different kinds, called isotopes, differing in atomic weight but not in chemical properties. Some isotopes are very rare naturally, and these can be used experimentally to follow the movements or change of combination undergone by an element when introduced into the body as part of a particular compound. For instance, heavy water is water containing an isotope of hydrogen. It can be used to follow the movement of water from one part of the body to another, or the chemical combinations undergone by hydrogen when it is introduced as water. Work with isotopes is made easier by using the numerous radioactive ones which physicists can produce, since their radioactivity gives them away and makes it easier to trace them.

MAMMALIA. A class of vertebrates characterised by fur (or hair), warm-bloodedness and by the fact that their young develop first within the mother and after birth are fed on milk (e.g. dog, elephant, whale, man).

NEMATODES. The round- or threadworms. Many are free-living in soil, etc. (e.g. vinegar eels), others are parasitic in plants (e.g. eelworm of potato and beet) or in animals (e.g. *Trichinella,* human hookworm).

NERVE FIBRE. The minute threads of protoplasm which conduct the impulses constituting nervous activity. Their diameter is usually between 1/1000 and 1/100 mm. Many thousands of them make up a nerve in a limb. The fibres of such a nerve connect sense organs to the central nervous system, and the central nervous system to muscles and glands. Similar fibres conduct impulses within the central nervous system.

OSMOTIC PRESSURE. When a solution of, say, sugar in water (but any dissolved substance or mixture of them will do) is separated from pure water by a membrane permeable to water but not to sugar, water passes across the membrane into the sugar solution. If external pressure is applied to the sugar solution, the movement of water into the sugar solution will be opposed. The pressure required to stop the movement completely is called the osmotic pressure of the sugar solution. It is greater the more concentrated the solution. Water will pass from a dilute solution to a strong one just as from pure water to a solution, provided the necessary membrane separates them.

PATHOGEN. Disease producing organism.

PLANKTON. A collective term for all small organisms living in the open sea.

PLASMA. *See* Blood.

POLYMORPHS. The most numerous kind of white cell of the blood.

POLYPEPTIDE. A product of the partial breakdown of a protein, consisting of numerous amino-acids, but not as many as in a protein.

PROTEIN. The most important compounds in living things. A protein molecule is very large and complex. It is built up from large numbers of units called *amino-acids*. About 25 different amino-acids are known. The varied combination of these amino-acids in a protein molecule (which may contain several hundreds of them) makes the number of possible kinds of protein almost infinite. The diversity is fully exploited by living things, and probably every individual has some unique protein molecules peculiar to itself.

PROTOZOA. Microscopic animal-like organisms, each consisting of a single cell.

RED BLOOD CORPUSCLE. *See* Blood.

REFLEX. A simple form of behaviour found in almost all animals. A stimulus applied to some sense organs (e.g. a pin stuck in the foot) causes impulses to pass up a group of nerve fibres into the central nervous system, where they are relayed through other nerve fibres, and impulses are set going down yet other nerve fibres which set in motion the muscles whose contraction withdraws the foot The withdrawal reflex is a function of the spinal cord, all the co-ordination being done there.

REPTILES. A class of cold-blooded vertebrates with dry scaly skins. In all living forms the large yolky eggs are laid on land and are protected by a thick shell. Examples of the class are snakes, lizards, tortoises and crocodiles.

SEBACEOUS GLAND. Small gland, secreting fatty substance, situated at the root of a hair.

SENSE ORGAN. The part of the nervous system which detects what goes on outside or inside the animal. Sense organs are of different kinds for the detection of different sorts of stimulus, such as light (eye), temperature (minute organs in the skin) or muscular movement (minute organs in muscles).

SERUM. The fluid obtained from clotted plasma after removal of the fibrin. Serum therefore will not clot.

SPECIES. Group of all animals or plants of the same kind; e.g. all domestic horses form one species. Similar species are grouped together into a *genus*. Similar genera are also grouped together, and so on in a hierarchy. Each species is known by a double scientific name, the first defining its genus, the second its species, e.g. *Rattus rattus* and *Rattus norvegicus* are two different *species* of the same *genus*. In some species different *varieties* can be recognised, from slight but constant differences of appearance or behaviour. The variety name is put after the specific name, e.g. *Rattus rattus frugivorus*.

TISSUE FLUID. The fluid (consisting of water, salts and a small amount of a variety of organic substances; *compare with* Blood) which fills the narrow crannies around cells and intercellular fibrils, outside but in contact with the blood-vessels. Tissue fluid bathes all cells of the body, and is the medium through which the cells receive diffusing food-stuffs and oxygen from the blood, and through which they pass their diffusible waste products to the blood.

VERTEBRATES. Animals with backbones. Includes the mammals, and also fishes, amphibia, reptiles and birds. *Invertebrates* have no backbone, e.g. insects, worms, snails, cuttlefish, starfish.

WHITE CELL. *See* Blood.

OUR CONTRIBUTORS

Anthony Barnett, M.A., is a zoologist who before the war specialised in embryology. Up to the end of 1940 he was working at Oxford on aspects of chemistry of embryonic development. For the past three years he has worked for the Government on the application of pest-control methods, mainly in England but recently also in Mediterranean areas where plague has been occurring.

Llewellyn Lloyd, D.Sc., has spent many years in research on problems connecting zoology with public health. He is an Honorary Member of the Institute of Sewage Purification and holds the appointment of Reader in Entomology and Protozoology in the University of Leeds.

R. F. Ewer, Ph. D., has worked on the function of invertebrate blood pigments. During the war she studied the biology of insects which infest stored foods. Her interest in whales is a hobby.

P. W. Brian, Ph.D., has been working on fungicides for Imperial Chemical Industries Ltd. since 1936. During the past three years he has been giving special attention to substances with fungicidal properties occurring naturally as metabolic products of micro-organisms.

Winifred E. Brenchley, D.Sc., Botanist, Rothamsted Experimental Station; author of *Manuring Grass Lands for Hay, Weeds of Farm Land, Inorganic Plant Poisons*, many scientific reports and papers, and (with H. C. Long) *Suppression of Weeds by Fertilisers and Chemicals.*

Harold C. Long, I.S.O., B.Sc. (Agric., Edin.). Ministry of Agriculture, 1904–38; Editor of the monthly Journal of the Ministry of Agriculture, 1914–38; author of *Common Weeds of the Farm and Garden, Plants Poisonous to Live Stock, Weeds of Grass Land,* Weeds of Arable Land,* Poisonous Plants on the Farm,* Suppression of Weeds by Fertilisers and Chemicals* (with Dr. W. E. Brenchley), and many papers and articles on farming subjects. (*Official Bulletins.)

Richard H. Knight, M.Sc., is Lecturer in Physics in the University of Birmingham. He is interested in the physics of biological problems, especially those concerned with the sense organs.

Michael Abercrombie, M.A., is Lecturer in Zoology in the University of Birmingham. He is especially interested in the medical aspects of biology, and has recently been researching on the changes which occur in severed nerves.

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